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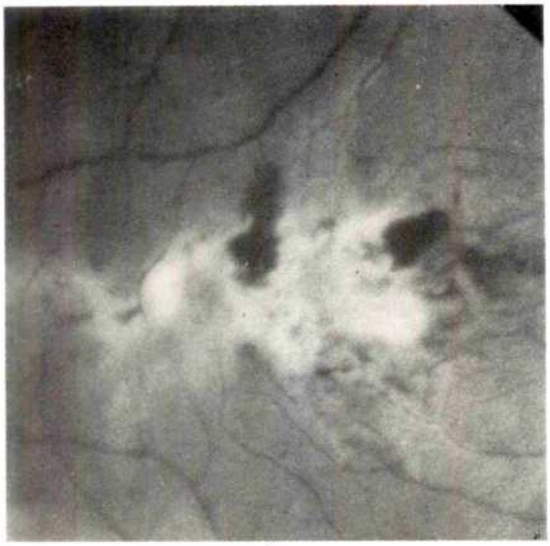

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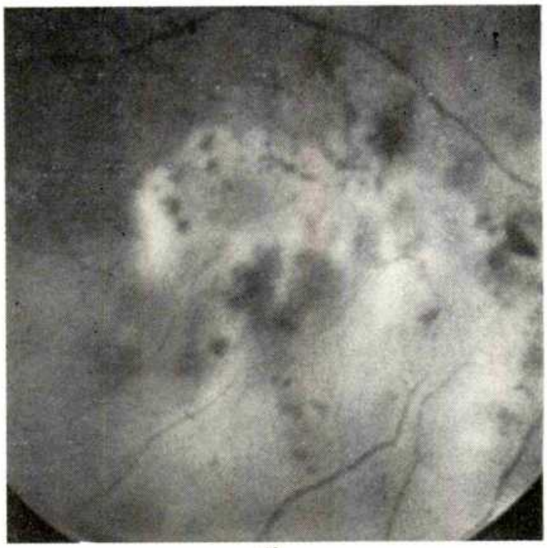

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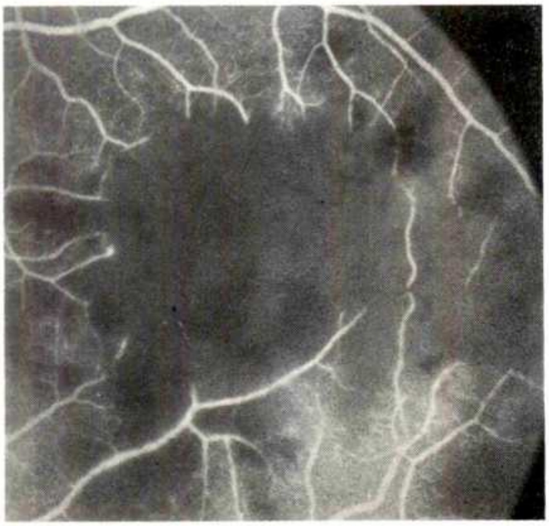

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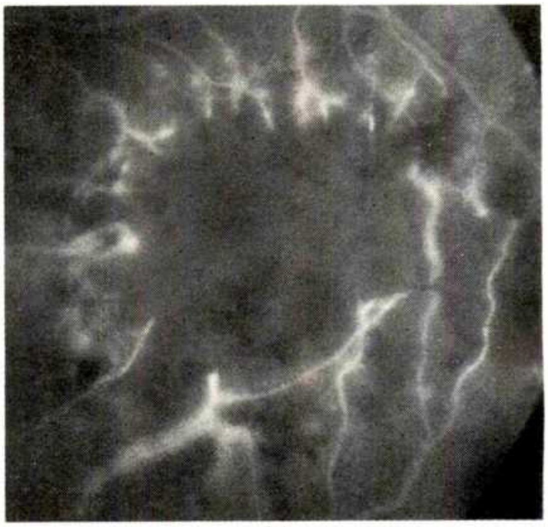

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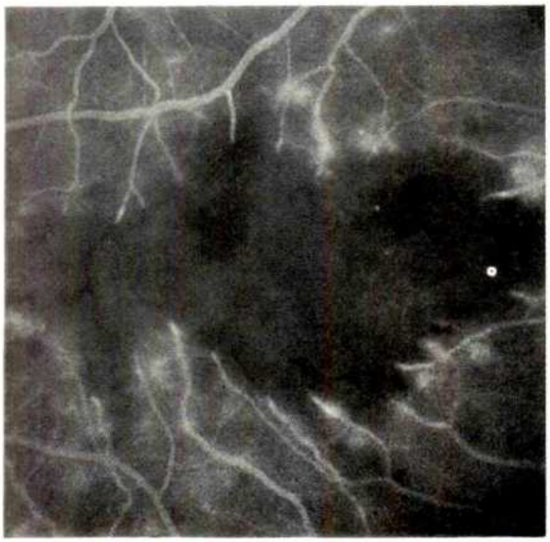

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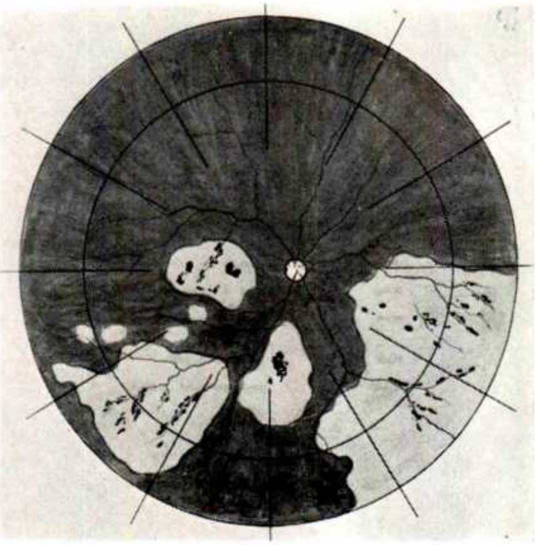

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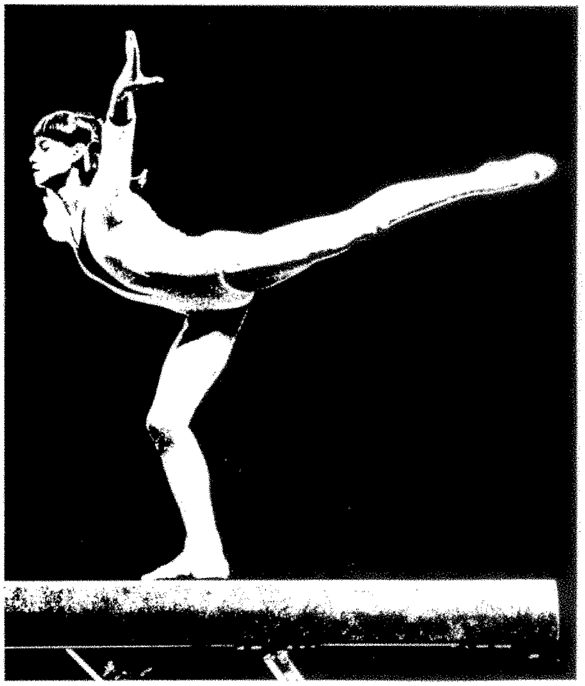

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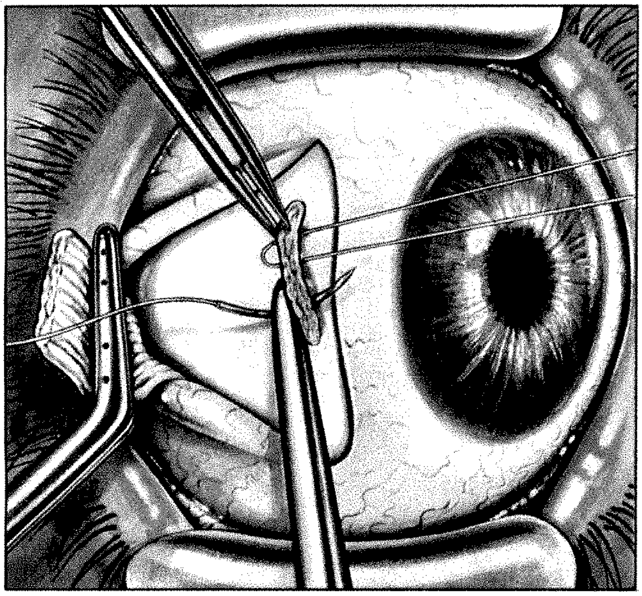

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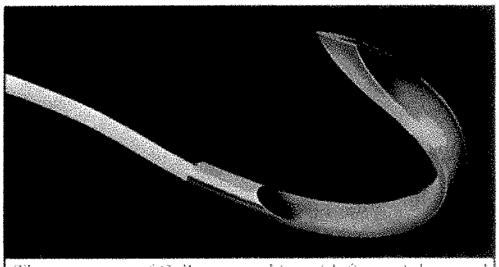

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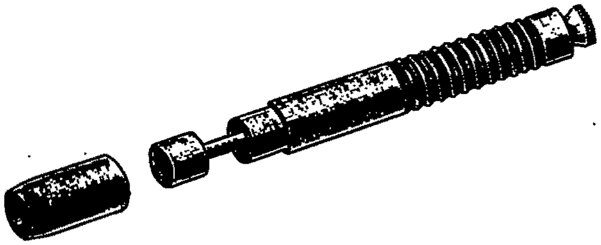

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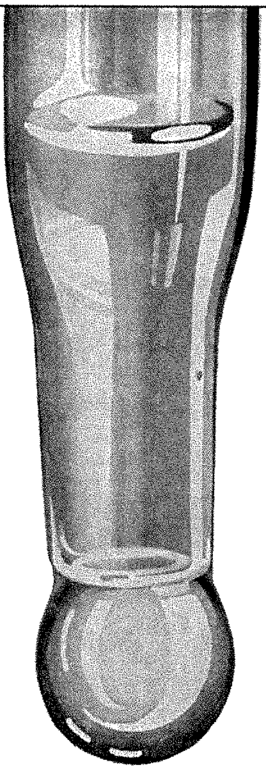

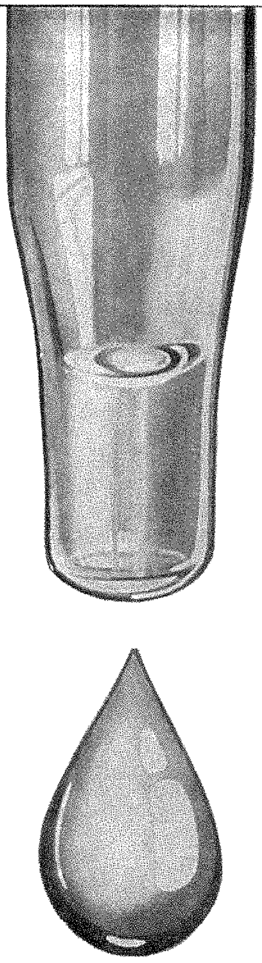

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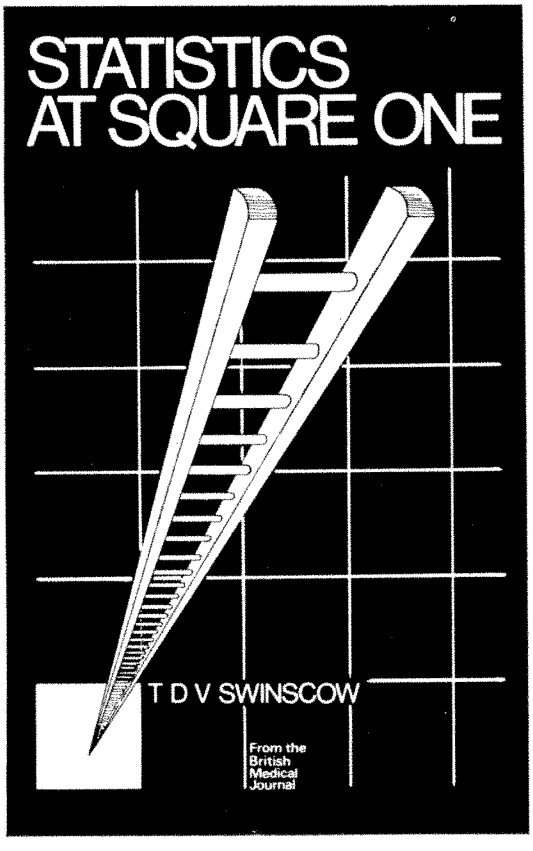

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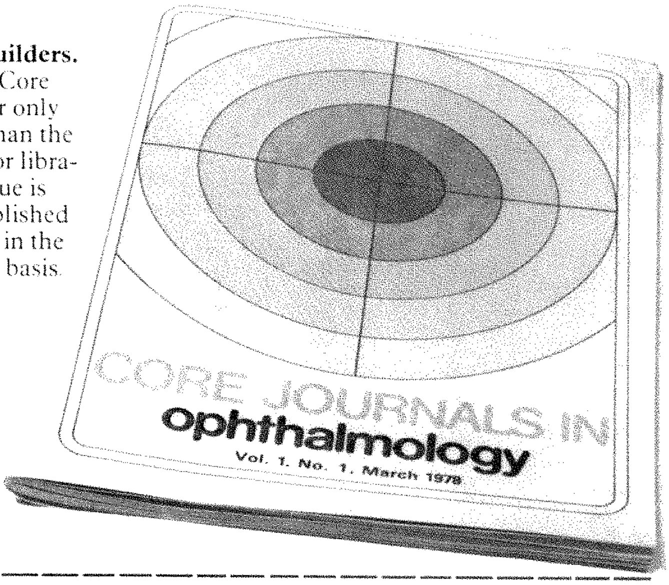

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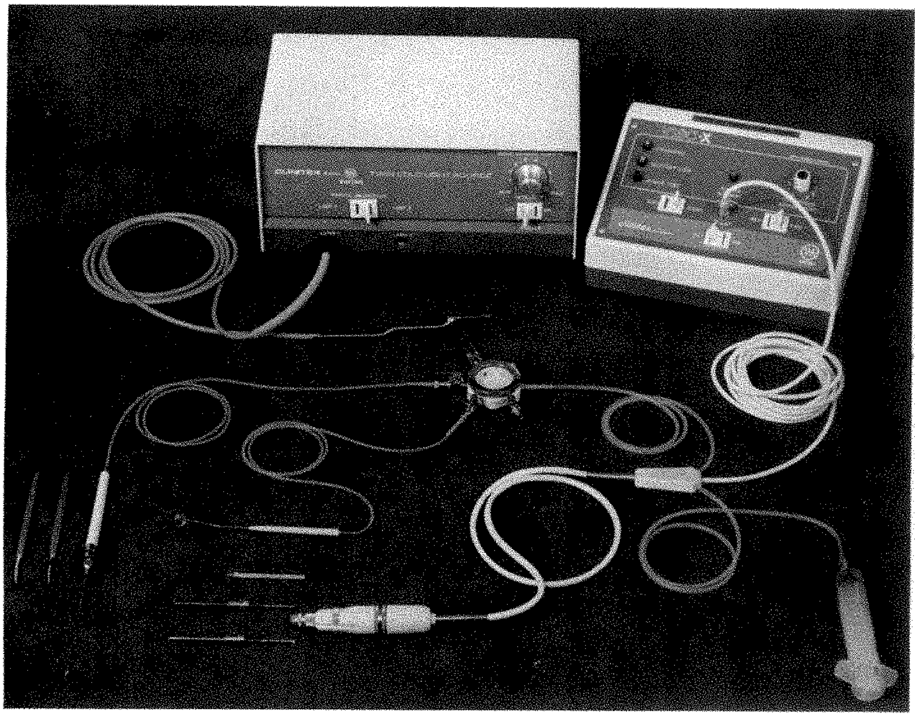

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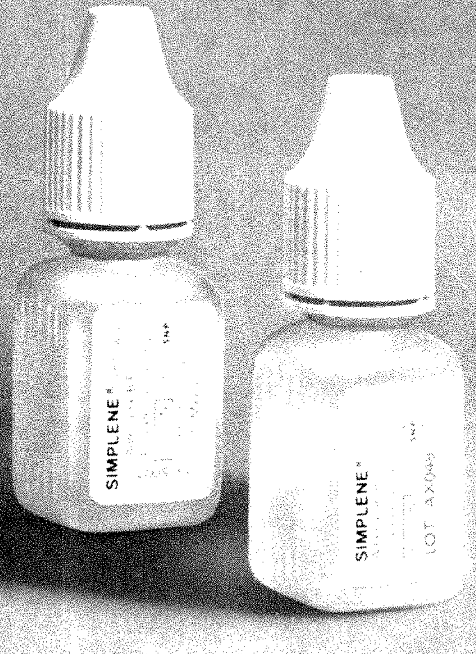

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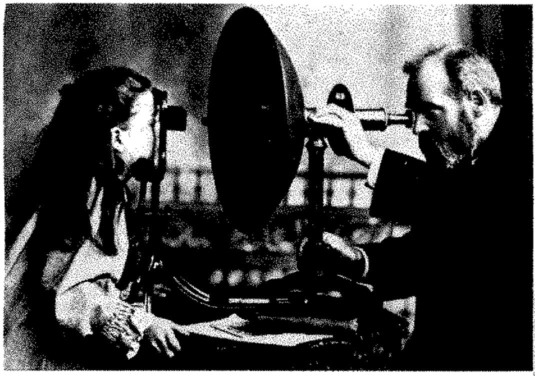

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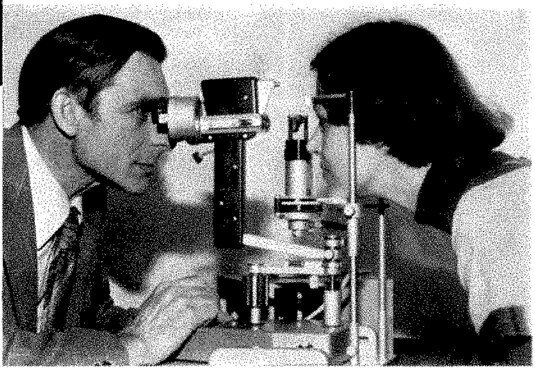

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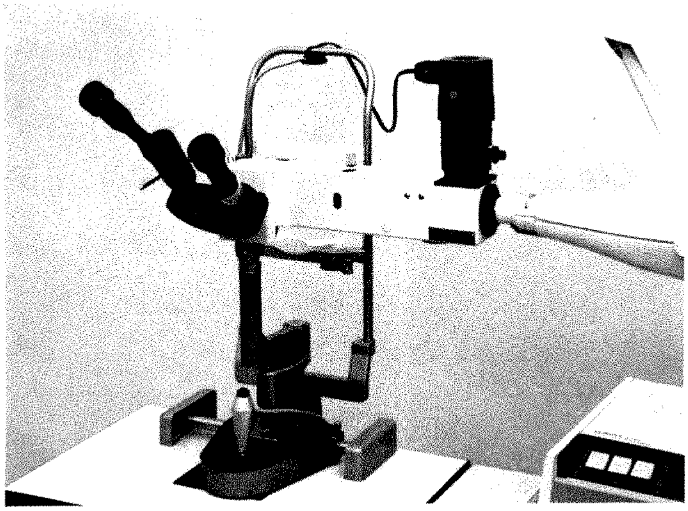

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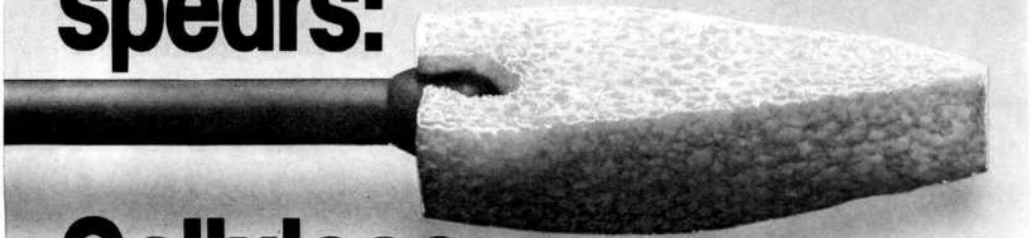

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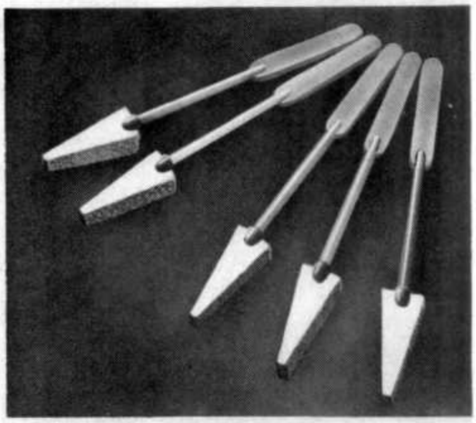

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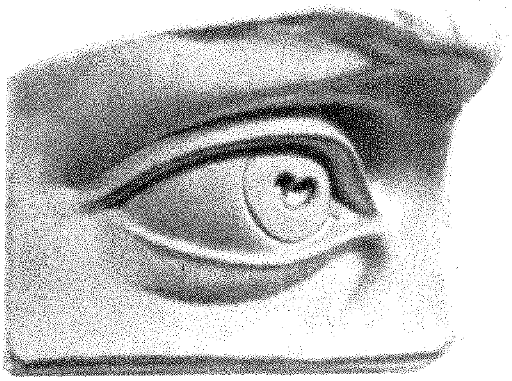

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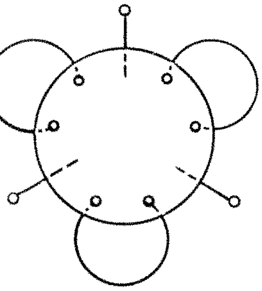

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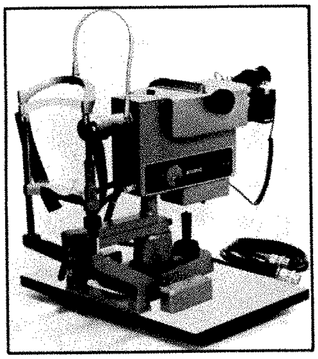

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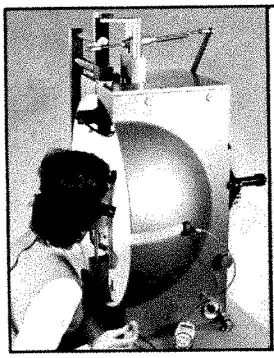

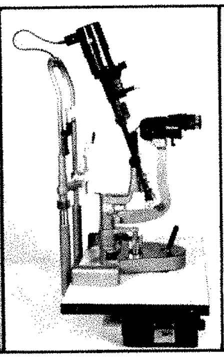

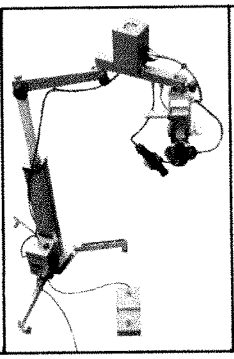

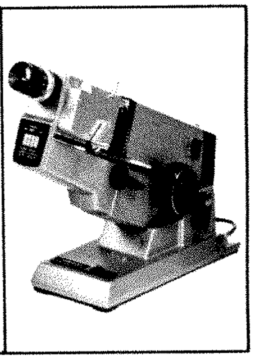

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Editorial: Pathogenesis of optic disc swelling

Swelling of the optic nerve head is a prominent ophthalmoscopic sign in a variety of ocular and systemic disorders including ischaemic optic neuropathy, raised intracranial pressure (papilloedema), accelerated systemic hypertension, and ocular hypotony. Recent experiments on primate models have led to a clearer understanding of the nature and pathogenesis of the disc changes in these disorders. Crucial to these advances have been investigations of the disturbed physiology of retinal ganglion-cell axons, which are the major constituent of the disc tissue.

The axonal swellings which develop adjacent to a ligation of an axon bundle result from interruption of the normal bidirectional transport of proteins and organelles within the axoplasm between the nerve-cell bodies and the synaptic terminals (Lubinska, 1964; Griffin *et al.*, 1977). The organelle-packed swellings on the cell-body side of the ligature are due to physical obstruction of continuing rapid orthograde transport (with a further contribution from obstructed slow orthograde flow), while the swollen stumps on the synapse side of the ligature result from obstructed retrograde flow. A similar transport block can also be produced by ischaemia, especially if this is sufficiently severe and prolonged to cause irreversible vacuolation and disintegration of a localised axon segment. In this issue Mr D. McLeod and colleagues (p. 591) present preliminary results which indicate that experimental occlusion of the posterior ciliary arterial supply to the optic nerve head causes infarction of the immediately retrolaminar myelinated optic nerve. The associated complete obstruction of rapid orthograde axoplasmic transport at the lamina cribrosa (as shown by autoradiography) is thought to be the fundamental cause of the opaque prelaminar swelling that characterises acute ischaemic optic neuropathy. The disc swelling is equivalent to a 'cotton-wool spot' of the optic nerve head. Like most retinal cotton-wool spots, the disc swelling does not itself represent ischaemic axon damage but is an accumulation of axoplasmic debris adjacent to an infarct (McLeod, 1976).

The site of obstruction of orthograde axoplasmic transport after posterior ciliary artery occlusion is the same as that found in experimental papilloedema due to implantation and inflation of intracranial balloons (Tso and Hayreh, 1977a). In papilloedema, however, the cause of the obstruction to rapid and slow axoplasmic transport at the lamina cribrosa is not so clearly defined. Hayreh (1976, 1977) believes that the obstruction is primarily mechanical and due to compression of the retrolaminar myelinated optic nerve by the raised pressure in the subarachnoid space, that is, equivalent to a partial ligature. Whatever the underlying mechanism, there is now good experimental evidence (Tso and Hayreh, 1977b) that the principal cause of the prelaminar swelling in papilloedema is distension of ganglion cell axons rather than intercellular or intraglial fluid accumulation as thought hitherto. Axonal distension is characteristic of even the earliest stages of disc swelling and is almost certainly a consequence, rather than the cause, of the axoplasmic transport block at the lamina. Thus, the swollen disc of papilloedema is truly a 'choked' disc in the axonal as well as the vascular sense. This concept is not incompatible with the preservation of vision in clinical papilloedema, since the transport block is incomplete and the axons are not disrupted and do not degenerate, at least in the early stages. The transport-block theory is also consistent with the observation that atrophic discs do not develop papilloedema, as in such cases there are no axons to swell.

Optic disc swelling with distended organelle packed axons also occurs in experimental systemic hypertension (Garner *et al.*, 1975). Although no physiological studies were performed, an axoplasmic transport block is undoubtedly implicated owing to either posterior ciliary ischaemia or raised intracranial pressure.

Axoplasmic transport has been thoroughly investigated in disc swelling from ocular hypotony and also in ocular hypertension, the overall effect of the latter being cupping rather than swelling of the optic disc (Anderson and Hendrickson, 1974; Minckler *et al.*, 1976; Minckler *et al.*, 1977; Minckler *et al.*, 1978). Again, an obstruction of slow and rapid orthograde axoplasmic flow has been demonstrated at the lamina cribrosa together with a retrograde transport block at the same site. From their detailed studies Minckler and colleagues conclude that the transport block is mechanical in nature, resulting from crimping of axons by the distorted glial-scleral columns of the lamina cribrosa.

There can be little doubt that the results of all these experiments have a direct bearing on optic disc swelling as seen clinically. An axoplasmic transport block appears to be the 'final common pathway' (Tso and Hayreh, 1977b) through which many ocular and extraocular disorders produce swelling of the optic nerve head.

References

Anderson, D. R., and Hendrickson, A. (1974). Effect of intraocular pressure on rapid axoplasmic transport in monkey optic nerve. *Investigative Ophthalmology*, **13**, 771–783.

Garner, A., Ashton, N., Tripathi, R., Kohner, E. M., Bulpitt, C. J., and Dollery, C. T. (1975). Pathogenesis of hypertensive retinopathy: an experimental study in the monkey. *British Journal of Ophthalmology*, **59**, 3–44.

Griffin, J. W., Price, D. L., Engel, W. K., and Drachman, D. B. (1977). The pathogenesis of reactive axonal swellings: role of axonal transport. *Journal of Neuropathology and Experimental Neurology*, **36**, 214–227.

Hayreh, S. S. (1976). Pathogenesis of optic disc oedema in raised intracranial pressure. *Transactions of the Ophthalmological Societies of the United Kingdom*, **96**, 404–407.

Hayreh, S. S. (1977). Optic disc oedema in raised intracranial pressure V. Pathogenesis. *Archives of Ophthalmology*, **95**, 1553–1565.

Lubinska, L. (1964). Axoplasmic streaming in regenerating and normal nerve fibres. *Progress in Brain Research*, **13**, 1–71.

McLeod, D. (1976). Ophthalmoscopic signs of obstructed axoplasmic transport after ocular vascular occlusions. *British Journal of Ophthalmology*, **60**, 551–556.

Minckler, D. S., Bunt, A. H., and Johanson, G. W. (1977). Orthograde and retrograde axoplasmic transport during acute ocular hypertension in the monkey. *Investigative Ophthalmology*, **16**, 426–441.

Minckler, D. S., Bunt, A. H., and Klock, I. B. (1978). Radioautographic and cytochemical ultrastructural studies of axoplasmic transport in the monkey optic nerve head. *Investigative Ophthalmology*, **17**, 33–50.

Minckler, D. S., Tso, M. O. M., and Zimmerman, L. E. (1976). A light microscopic autoradiographic study of axoplasmic transport in the optic nerve head during ocular hypotony, increased intraocular pressure and papilloedema. *American Journal of Ophthalmology*, **82**, 741–753.

Tso, M. O. M., and Hayreh, S. S. (1977a). Optic disc oedema in raised intracranial pressure IV. Axoplasmic transport in experimental papilloedema. *Archives of Ophthalmology*, **95**, 1458–1462.

Tso, M. O. M., and Hayreh, S. S. (1977b). Optic disc oedema in raised intracranial pressure III. A pathological study of experimental papilloedema. *Archives of Ophthalmology*, **95**, 1448–1457.

CASE 2

A 57-year-old female was first seen on 9 March 1974 with a 2-day history of watering and aching of the right eye. Visual acuity was 6/6 part with each eye. In the right eye there was anterior uveitis with large keratic precipitates and raised intraocular pressure. There was a cellular reaction in the vitreous with confluent yellowish-white swelling of the peripheral retina, especially below. The left eye was normal at this time. She was treated with local cycloplegics and corticosteroids, but 1 week later systemic antibiotics and corticosteroids were introduced as the changes became more marked.

Two weeks after initial presentation she developed

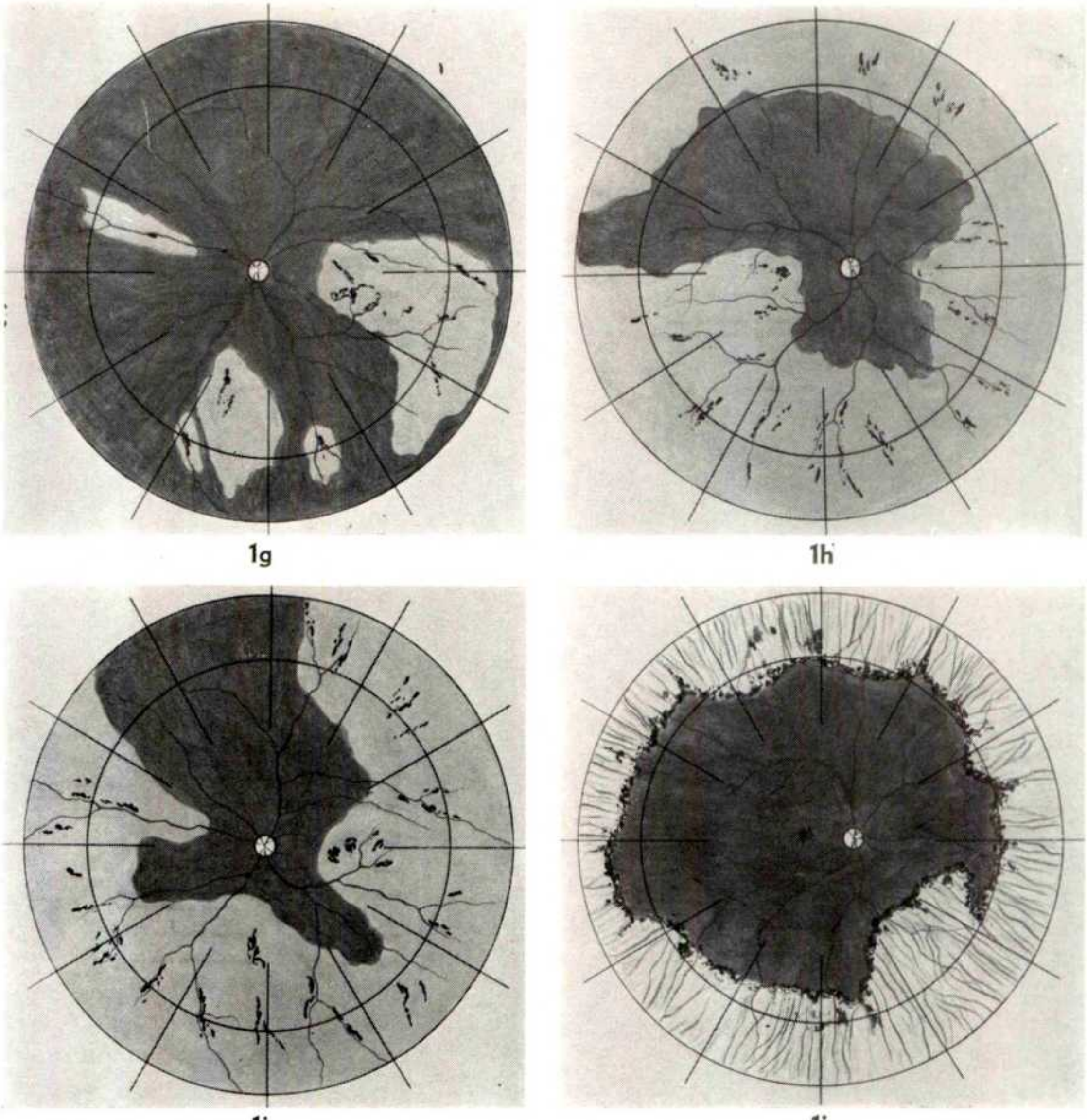


Fig. 1 *Case 1—Retinal swelling and haemorrhages of both maculae, 22 September 1971* (1a, b). *Fluorescein angiograms show no perfusion of the retina with leakage of the vessels at the margins of retinal non-perfusion (left eye* 1c, d; *right* eye 1e). *Retinal diagrams showing distribution of disease 27 September 1971* (1f, g), *4 October 1971* (1h, i), *and 5 March 1972* (1j)

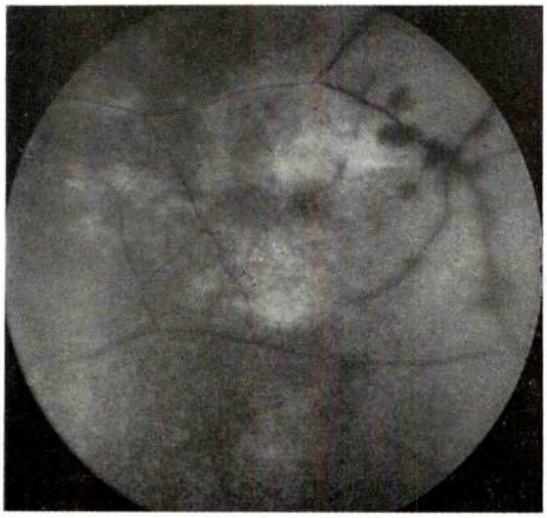
anterior uveitis, with raised intraocular pressure in the left eye, with vitreous cells and confluent peripheral yellow retinal swelling with perivascular haemorrhages (Figs. 2*a*, *b*). The vision at that time was hand movements with the right eye and 6/18 with the left.

Fluorescein angiography of the left temporal retina showed perfusion to be normal in the unaffected retina but no perfusion in the diseased retina, where the blood vessels appeared to have stagnant blood columns. There was hyperfluorescence of the vessel walls at the margins of the lesions. In the areas of retinal non-perfusion intraretinal dye was seen early in the study and was presumed to be derived from the choroid (Fig. 2*c*).

Investigations
Hb, PCV, WBC, urea, and electrolytes were normal. Immunoglobulins were reported initially as being generally decreased but subsequently as normal. Blood cultures were sterile, and there was no serological evidence of syphilis, toxoplasmosis, or rheumatoid arthritis. Chest and skull x-rays were normal.

The ESR was repeatedly raised, and this prompted a full investigation for a systemic disorder, but none was detected.

Progress
One month after presentation the vitreous in each eye continued to show a heavy cellular reaction but was sufficiently clear to see the entire pre-equatorial region of each fundus replaced by a yellowish-white infiltration with a sharp posterior line of demarcation. Within areas of disease patches of apparent resolution could be seen which were also well defined. There were a few scattered haemorrhages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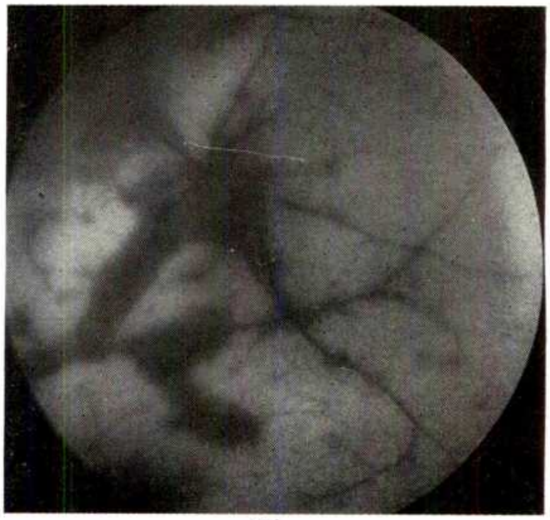
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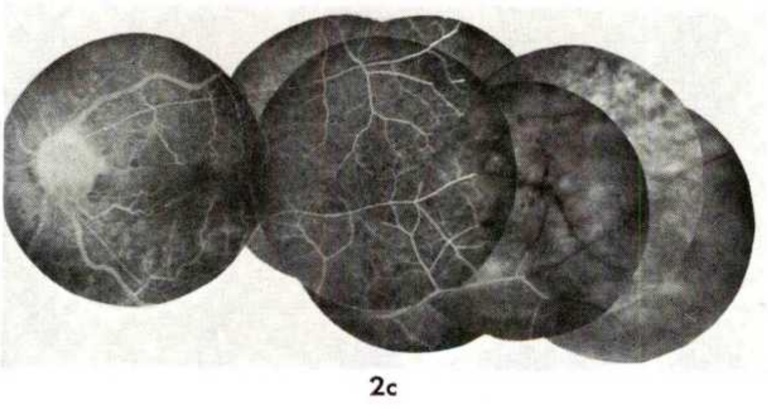

2c

Fig. 2 *Case 2—Swelling and haemorrhages in the left temporal retina on 1 April 1974* (2a), *which increased considerably by 3 April 1974* (2b). *Fluorescein angiography showed no perfusion of the affected retina* (2c)

within the lesion. Systemic corticosteroid therapy was continued and the dose increased.

Three weeks later the vision in the right eye had improved to 6/18. Minimal inflammation was present in both anterior segments, with a few cells and considerable debris in the vitreous of each. No retinal swelling could be seen, but in its place was well demarcated retinal pigment epithelial change. The retinal vessels were extensively sheathed and were narrow on fluorescein angiography.

Four days after this assessment she developed a detachment of the left retina, apparently due to the retina tearing along the posterior demarcation of the previously infiltrated retina. This was considered inoperable as the dehiscence extended through 360°.

Three months after initial presentation she developed a detachment of the temporal half of the right retina due to a tear in the upper temporal quadrant and a dehiscence of the retina below, again along the posterior demarcation of the chorioretinal scarring. This was treated by encirclement, drainage of subretinal fluid, cryotherapy, and intravitreal air injection, but she developed signs of anterior segment ischaemia, which failed to resolve, and both eyes are now blind and becoming phthisical.

CASE 3

A 58-year-old male electrical inspector presented on 4 June 1975 with a 1-week history of redness, pain, and blurring of vision in the right eye starting immediately prior to the onset of acute urinary retention. Right eye vision was 6/60 with a moderate anterior uveitis and normal intraocular pressure. There was massive vitreous exudation with debris and cells. In the fundus were widespread scattered areas of grey to white swollen retina in the mid periphery, which became confluent more anteriorly and were associated with multiple small haemorrhages. The left eye was normal with a vision of 6/6.

Over the next 2 weeks the right eye subjectively improved on local corticosteroids, but the left developed a mild anterior uveitis with raised intraocular pressure. After a further 10 days left eye vision fell to 6/12 with many cells appearing in the vitreous, and the retina developed similar changes to those seen in the right eye, with narrowing and sheathing of the peripheral arterioles, which were partly obscured by the opaque retina. This eye was also treated with local and orbital floor corticosteroids.

Fluorescein angiography was of poor quality on account of the large amount of vitreous activity, and no conclusions could be drawn concerning the

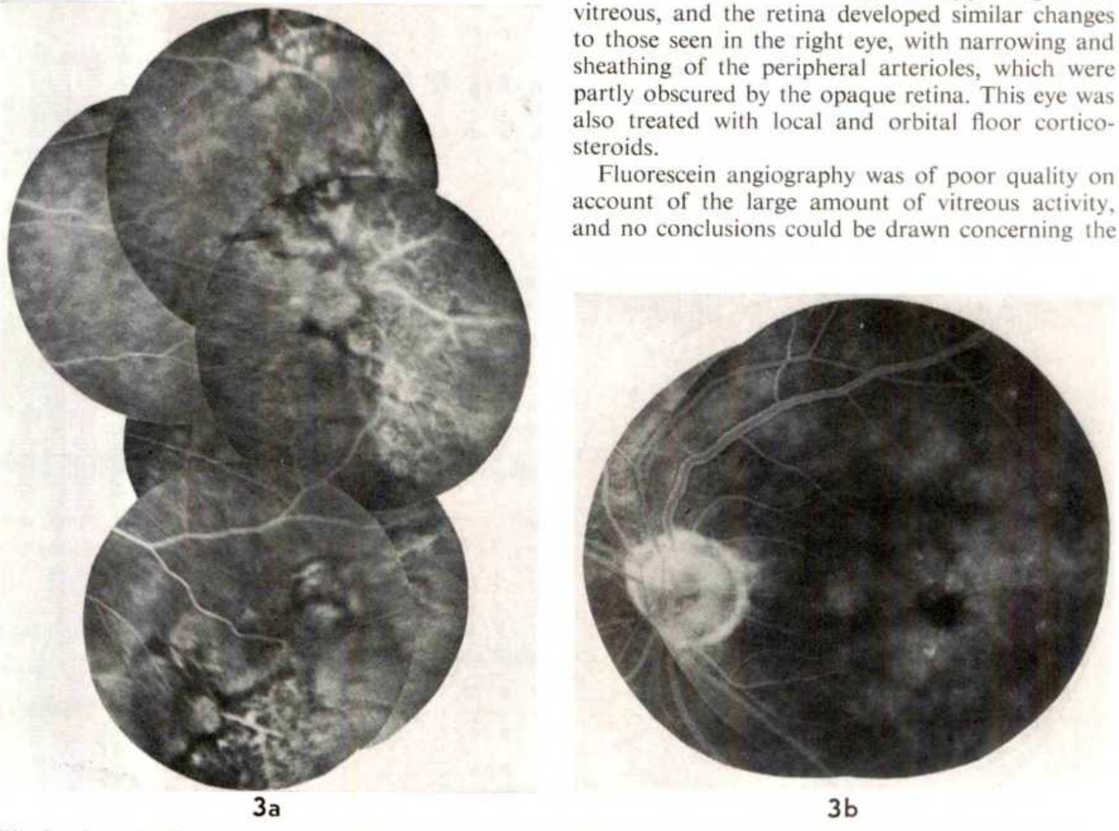
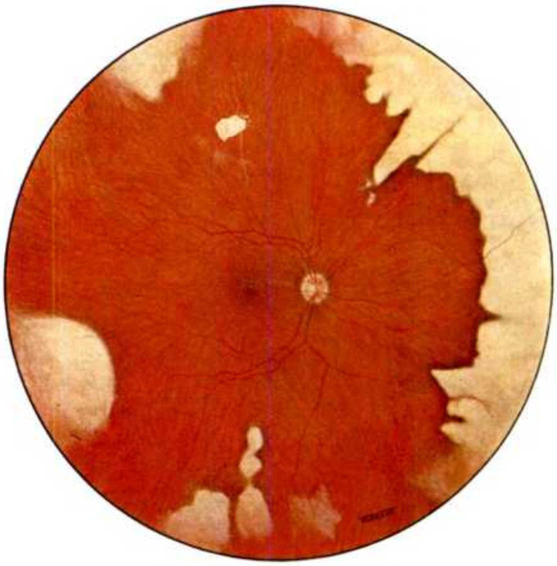

3a
3b

Fig. 3 *Case 3—Fluorescein angiography on 11 September 1975 after resolution of the disease showing peripheral transmission defects* (3a) *and cystoid macular oedema* (3b)

retinal circulation. Five minutes after dye entry there was considerable dye accumulation in the peripheral retina of the right eye.

Investigations
The following were normal: Hb, PCV, WBC, serum calcium, lipoproteins, total plasma proteins, and serology for syphilis. The gammaglobulin fraction was raised, with a slight increase in IgM and IgA. Anti-smooth muscle antibody was detected in a 1:10 dilution. Blood cultures were sterile. The toxoplasma dye test was positive at 1/64 dilution, but no rising titre and 2 blood samples for cytomegalovirus complement fixation test showed a titre of <1/8. The ESR was raised at 46 mm/h. A chest *x*-ray showed minor emphysematous changes, but the lumbar spine and sacroiliac joints showed the changes of advanced ankylosing spondylitis.

Fig. 4 *Case 4—Dense yellow swelling of the periphera retina on 28 January 1977. In the right eye* (4a) *this co-existed with areas of pigment epithelial change where swelling had resolved. In the left eye* (4b) *the acute lesions were associated with haemorrhages and there was vitreous debris. After resolution areas of swelling were replaced by well-defined retinal pigment epithelial atrophy in the right eye (9 June 1977)* (4c, d). *Fluorescein angiography on 1 June 1977 showed dilated perifoveal capillaries* (4e) *and cystoid macular oedema* (4f)



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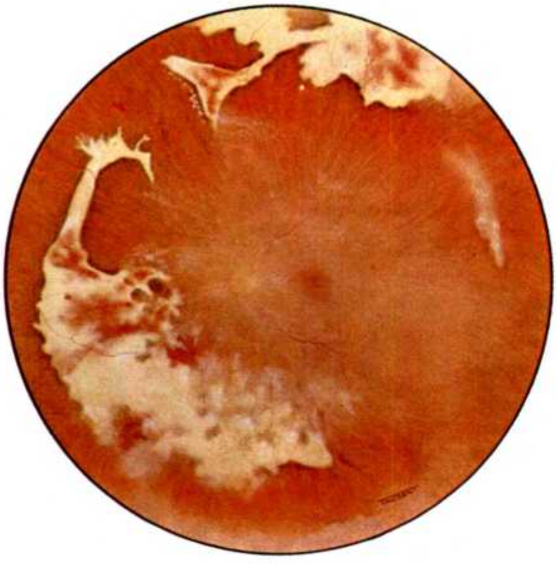

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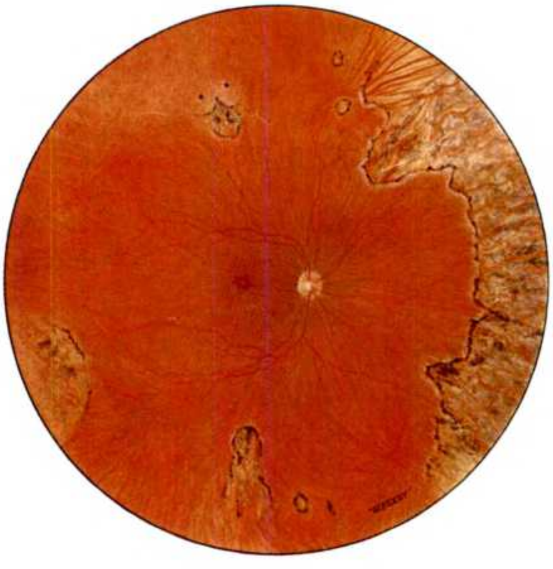


4c

No evidence of vasculitis was seen in a conjunctival biopsy on electron microscopy.

Progress

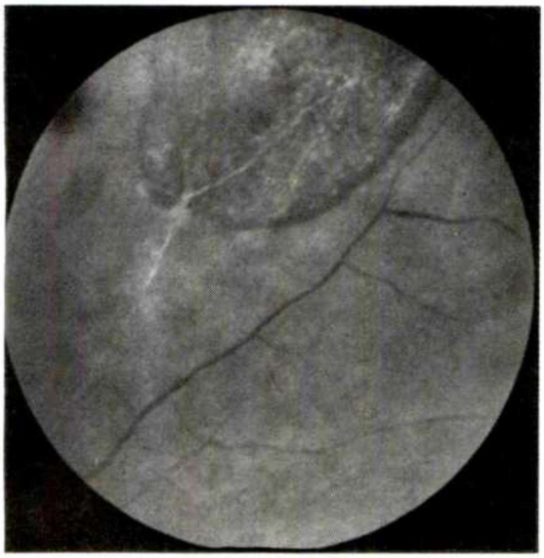
Over the next month areas of retinal swelling disappeared in a patchy manner and the vitreous opacity increased. Ten weeks after initial presentation the patient developed a subtotal detachment of the right retina. There was marked reduction in vitreous mobility in this eye, with increase in debris and cells; the retina developed massive periretinal fibrosis and failed to re-attach after surgery. At this time vision with the left eye was 6/9, with minimal signs of anterior uveitis. There was vitreous debris and in the retinal periphery a geographic pattern of fine pigmentary change at the sites of previous inflammation. There was widespread peripheral vessel closure.

Fluorescein angiography confirmed the sharp transition from normal to abnormal retina, but there was no dye leakage (Fig. 3*a*) apart from macular oedema (Fig. 3*b*).

When last assessed on 12 February 1977 the left eye had an acuity of 6/12, reading N5, and showed no signs of active disease, with no change in the retinal pigmentary pattern.

CASE 4

A 58-year-old retired medical practitioner was first seen by Mr S. P. Redmond in Lincoln on 13 December 1976 with a 10-day history of sudden redness of the left eye followed by deterioration of vision. This had been preceded by a feverish illness the day before. A diagnosis of iritis with raised intraocular pressure was made, and later he developed signs of posterior uveitis. He was treated with local and systemic corticosteroids, but 6 weeks later developed similar symptoms in the right eye. When referred to Moorfields Eye Hospital on 20 January 1977, 2 days after the right eye had become affected, the right vision was 6/12 and the left 6/18. Both anterior chambers showed a moderate uveitis with normal intraocular pressures. There was cellular reaction and debris in each vitreous, which



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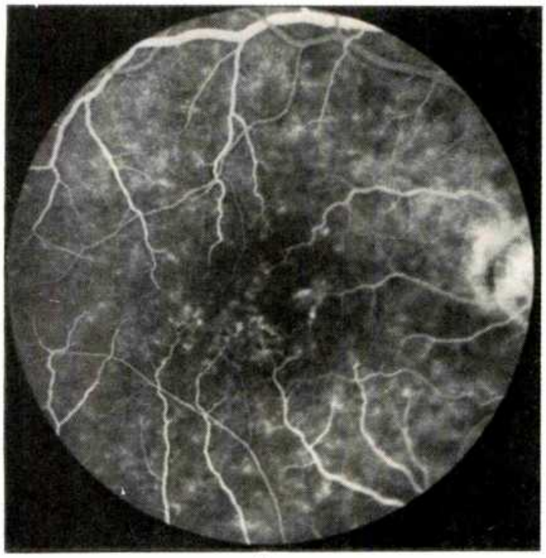

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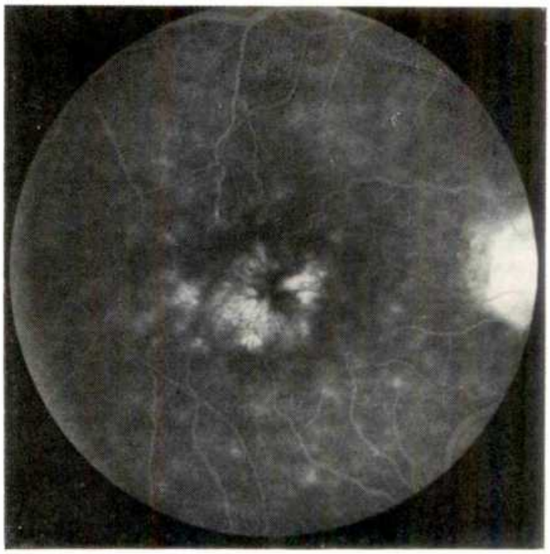

4f

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was more marked in the left. In both fundi there was confluent yellowish-white retinal swelling in the periphery with haemorrhages (Fig. 4*a*, *b*). In the right eye gaps existed within the areas of swelling, in which there were mild retinal pigment epithelial changes.

Investigations

Clinical examination showed no signs of systemic disease. Blood cultures were sterile and serological tests for syphilis and toxoplasmosis were negative. The blood chemistry was normal, as was the ESR. The only abnormality in the protein fractions was a slightly raised gammaglobulin, but the immunoglobulins were normal. The Hb was 17·4 g/dl, PCV 53%, WBC $13{\cdot}0\times10^9$/l, the differential count showing a lymphocytosis. Antinuclear factor was detected, 1:40, and the cytomegalovirus complement fixation titre was 1:64, but not rising. His chest and skull were normal on *x*-ray.

Progress

The patient was treated with local and systemic corticosteroids, and during the next 4-week period gaps progressively appeared in the areas of disease, which were replaced by retinal pigment epithelial changes only. Within these areas the retinal blood vessels were sheathed and were not perfused.

On 23 February 1977 he was reviewed as the left eye vision had deteriorated for the previous 2 days. At this time the right vision was 6/9 with a quiet anterior chamber and fine pigment stippling in the peripheral retina in the areas of previous inflammation. Left vision, however, had dropped to hand movements, and there was a marked increase in the vitreous debris obscuring the disc and macula; the peripheral retina showed a white plaque in the inferonasal quadrant. His corticosteroid dose was increased but despite this the eye worsened and he developed a traction detachment of the posterior retina. When last reviewed on 1 June 1977 the right eye, in which the vision has improved to 6/5, now had a vision of 6/12. The anterior chamber of this eye was clear and there were vitreous cells. There were well-demarcated areas of subtle retinal pigment epithelial change in the periphery and macular oedema (Fig. 4*c*, *d*). Fluorescein angiography of the right eye demonstrated dilatation of the perifoveal capillaries (Fig. 4*e*) with leakage of dye into the retina (Fig. 4*f*). In the left eye there were peripheral retinal pigment epithelial changes and a retinal detachment arising from a retinal dehiscence above, beyond which the retina appeared to be absent.

ADDENDUM

While this paper was in preparation a further patient was seen in whom the findings suggested similar disease to that described in the other 4 cases. At the time of examination he had a total detachment of the right retina (Fig. 5) and very subtle retinal pigment epithelial disturbances in the periphery of the left eye.

SUMMARY OF DISEASE PROCESS

All the eyes of these patients had bilateral peripheral retinal change and, in 1, bilateral macular disease. The swollen retina was intensely opaque and yellowish-white with a well demarcated border between normal and abnormal retina. Fluorescein angiography showed no capillary perfusion in the affected areas, with dye leakage from the few surviving major vessels crossing non-perfused retina and at the terminations of the occluded larger vessels as they entered the swollen tissue. Shortly afterwards areas of diseased retina cleared in a patchy manner, leaving mild retinal pigment epithelial changes only. The vessels within this area became sheathed, and in most perfusion was not re-established. Clearing of the diseased retina was accompanied by marked accumulation of vitreous debris. It was thought that clearing was due to retinal necrosis, with sloughing of the retina into the vitreous. In 5 of the 8 eyes the retina became detached with tears at the demarcation between normal and abnormal retina.

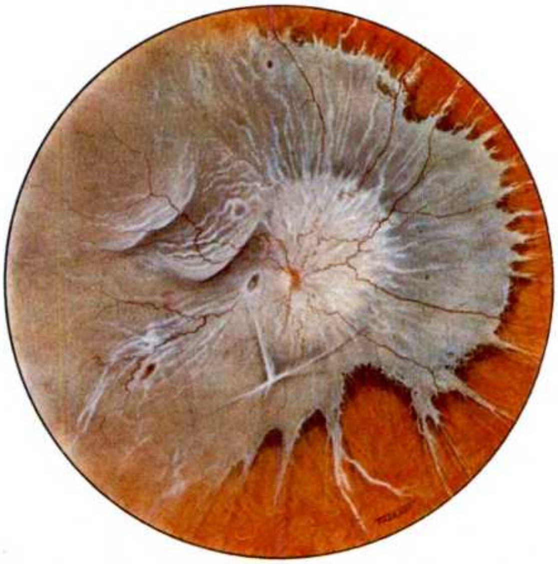


Fig. 5 *Retinal detachment with periretinal fibrosis and discontinuous retinal tears through 210° of the retinal periphery*

this tended to support the concept that the retina was largely deficient beyond the demarcation line. In none of these eyes was retinal re-attachment achieved.

The choroid appeared normal during the acute phase of the disease and there was no evidence of choroidal vessel closure at the time of acute disease, but atrophy of the choriocapillaris has occurred in the previously diseased areas in the first case now followed for 6 years.

The disease was characteristically bilateral and symmetrical, although 1 eye was involved before the other in all cases. Apart possibly from Case 4 this disease occurred as a single acute attack without recurrence. No systemic abnormalities were identified in any patient to indicate the cause of the disease.

Discussion

In the absence of any clinical or histopathological evidence to indicate the nature of the disease, its aetiology remains obscure. Retinal vascular non-perfusion in the affected areas suggests the possibility of infarction. However, retinal infarction due to retinal vascular disease alone is characterised by mild grey opacity of the retina as opposed to the dense opacity seen in these patients. The resolution of ischaemic swelling is fairly rapid and the retinal pigment epithelial changes are mild or absent. The intense opaque white lesions seen in infarcted retina due to accumulation of axoplasmic debris (McLeod, 1976) are characteristically linear and not seen in the peripheral retina. Choroidal infarction alone causes sector-shaped retinal swelling (Amalric, 1971; Foulds *et al.*, 1971); resolution of swelling is rapid and results in marked atrophy of the retinal pigment epithelium and choriocapillaris. Infarction due to coincident obstruction of both choroidal and retinal circulations gives rise to intensely opaque white swollen retina as seen in our patients. The period of resolution, however, is shorter and the choroidal changes much more marked, with atrophy of the pigment epithelium and choriocapillaris and migration of pigment-containing cells into the retina. It seems unlikely, therefore, that the disease which we have described is due to vascular occlusion alone.

In Behçet's syndrome the retinal disease is produced by a combination of vasculitis and infarction. The fluorescein findings are similar in many respects to those of our cases, with an accumulation of white exudative material in the deep retina and obscuration of the retinal vascular pattern in these areas (Shimizu, 1972). The posterior pole is the site most commonly affected in this disease, whereas the periphery was usually involved in ours.

Alternatively, this disease may be the result of retinitis due to an infective agent. The evolution of the disease suggests primary involvement of the neuroretina rather than spread from the neighbouring structures. The distribution of the lesions and the self-limited course are unlike bacterial infection, and no source of bacterial infection was detected in any patient. Virus infections produce a primary retinitis. The retinitis of cytomegalic inclusion disease (CID) at its height is clinically indistinguishable from BARN (de Venecia *et al.*, 1971). Scattered white dots or white granular patches are seen early on, and these become confluent with the development of haemorrhages. During the healing phase there is atrophy of the retina and pigmentary changes in the retinal pigment epithelium. Histologically there is massive coagulative necrosis of the retina, with little inflammation; the pigment epithelium and choroid are affected little by the disease or not at all (Smith, 1964; Wyhinny *et al.*, 1973; Chumbley *et al.*, 1975). The pattern of disease in CID retinitis is unlike BARN. The cases described in this paper had simultaneous affection of large areas of retina, and the extent of the disease was determined within a short time of onset. By contrast CID causes slowly spreading disease of the retina over a period of weeks, so that the swelling of acute disease is seen at the same time as pigment epithelial atrophy in old lesions; usually the whole retina is affected eventually. Moreover, of the many patients described with CID only one was not immunodeficient (Chawla *et al.*, 1976). Our patients showed no positive evidence of CID infection and none was immunodeficient.

Necrotising retinitis may also be produced by herpes simplex virus infection with relative sparing of the choroid (Cogan *et al.*, 1964; Cibis, 1975), but such cases rarely occur except during infancy (Pavan-Langston and Brockhurst, 1969). A case of retinitis following herpes zoster ophthalmicus has been described by Brown and Mendis (1973) in which extensive peripheral yellow retinal exudates were associated with attenuated retinal arterioles, but without haemorrhages. Measles retinitis is rarely seen in the absence of subacute sclerosing panencephalitis (Nelson *et al.*, 1970).

The descriptions of viral retinitis demonstrate close morphological similarities with BARN and suggest that the disease described in our patients may be due to primary retinitis, probably of an infective aetiology. However, no clinical evidence was identified which might indicate the infective agent.

Experimental autoimmune retinitis has been produced in animals (von Sallmann *et al.*, 1969), but such a disease process remains a theoretical possibility at present.

Two cases were reported by Willerson *et al.* (1977) in which the peripheral retinal changes were almost indistinguishable from the patients we have described, both in the fundus appearances and in the evolution of the disease; in all 4 of their eyes the retina became detached and failed to respond to surgery. In neither patient was an aetiology identified beyond question. Both had some stigmata of Behçet's disease and 1 developed herpes simplex dermatitis when on antimetabolite and corticosteroid therapy. There was insufficient evidence in either patient for Behçet's disease to be diagnosed with certainty, nor could herpes simplex retinitis be confirmed conclusively, since the cytopathic effects typical of the virus could not be produced on tissue culture with the subretinal fluid obtained from 1 patient.

Bilateral acute retinal necrosis appears to be a definite and recognisable clinical entity in which the course of the disease can be predicted. Treatment does not appear to alter its course.

We thank Mr Barrie Jay, Mr R. A. Hitchings, and Mr P. K. Leaver for allowing us to study and publish their cases. We are particularly grateful to Mr K. Sehmi for photographic assistance and to Miss J. Fisher for secretarial help.

References

Amalric, P. (1971). Acute choroidal ischaemia. *Transactions of the Ophthalmological Societies of the United Kingdom*, **91**, 305–322.

Brown, R. M., and Mendis, U. (1973). Retinal arteritis complicating herpes zoster ophthalmicus. *British Journal of Ophthalmology*, **57**, 344–346.

Chawla, H. B., Ford, M. J., Munro, J. F., Scorgie, R. E., and Watson, A. R. (1976). Ocular involvement in cytomegalovirus infection in a previously healthy adult. *British Medical Journal*, **2**, 281–282.

Chumbley, L. C., Robertson, D. M., Smith, T. F., Campbell, R. J. (1975). Adult cytomegalovirus inclusion retino-uveitis. *American Journal of Ophthalmology*, **80**, 807–816.

Cibis, G. W. (1975). Neonatal herpes simplex retinitis. *Albrecht von Graefes Archiv für klinische und experimentelle Ophthalmologie*, **196**, 39–47.

Cogan, D. G., Kuwabara, T., Young, G. F., and Knox, D. L. (1964). Herpes simplex retinopathy in an infant. *Archives of Ophthalmology*, **72**, 641–645.

de Venecia, G., Zu Rhein, G. M., Pratt, M. V., and Kisken, W. (1971). Cytomegalic inclusion retinitis—A clinical, histopathologic and ultrastructural study. *Archives of Ophthalmology*, **86**, 44–57.

Foulds, W. S., Lee, W. R., and Taylor, W. O. G. (1971). Clinical and pathological aspects of choroidal ischaemia. *Transactions of the Ophthalmological Societies of the United Kingdom*, **91**, 323–341.

McLeod, D. (1976). Ophthalmoscopic signs of obstructed axoplasmic transport after ocular vascular occlusions. *British Journal of Ophthalmology*, **60**, 551–556.

Nelson, D. A., Weiner, A., Yanoff, M., and de Peralta, J. (1970). Retinal lesions in subacute sclerosing panencephalitis. *Archives of Ophthalmology*, **84**, 613–621.

Pavan-Langston, D., and Brockhurst, R. J. (1969). Herpes simplex panuveitis—A clinical report. *Archives of Ophthalmology*, **81**, 783–787.

Shimizu, K. (1972). Fluorescein fundus angiography in Behçet's syndrome. *Modern Problems in Ophthalmology*, **10**, 224–228.

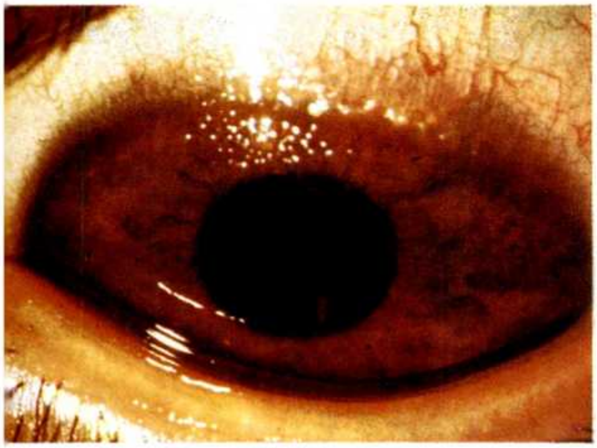
Smith, M. E. (1964). Retinal involvement in adult cytomegalic inclusion disease. *Archives of Ophthalmology*, **72**, 44–49.

Von Sallmann, L., Meyers, R. E., Stone, S. H., and Lerner, II, E. M. (1969). Retinal and uveal inflammation in monkeys following inoculation with homologous retinal antigen. *Archives of Ophthalmology*, **81**, 374–382.

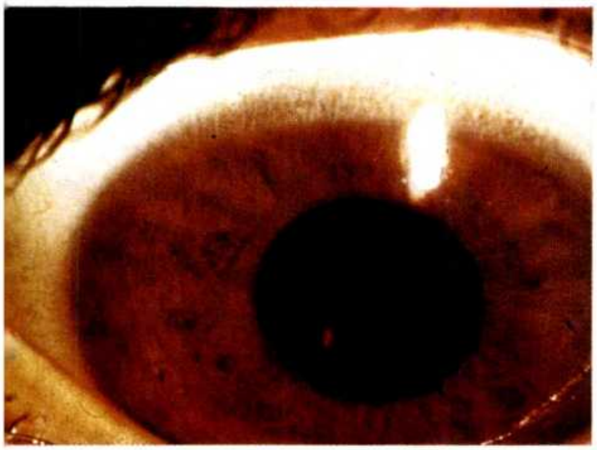
Wyhinny, G. J., Apple, D. J., Guastella, F. R., and Vygantas, C. M. (1973). Adult cytomegalic inclusion retinitis. *American Journal of Ophthalmology*, **76**, 773–781.

Willerson, Jr., D., Aaberg, T. M., and Reeser, F. H. (1977). Necrotizing vaso-occlusive retinitis. *American Journal of Ophthalmology*, **84**, 209–219.

In his eyes, allergy is much more than a minor irritation.



The superior limbus in a placebo treated eye of a patient suffering from ernal kerato-conjunctivitis, stained with fluorescein. Note the limbal yperaemia and swelling and the irregularity of the corneal surface.



The opposite eye of the same patient treated with sodium cromoglycate e drops. Before treatment, both eyes appeared similar.

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Fundus signs in temporal arteritis

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SUMMARY A patient with temporal arteritis developed a variety of ischaemic lesions in the eyes. Infarction of the inner retina and optic nerve head was delineated on presentation by white swelling in the retinal nerve fibre layer. The role of interrupted axoplasmic transport in the production of this sign is discussed. Outer retinal infarction was also noted on presentation and subsequently gave rise to striking pigmented scars.

Temporal arteritis often presents with visual loss, and necropsy examination in such cases shows widespread disease of the ophthalmic artery and the extraocular course of its ciliary and retinal branches (Henkind *et al.*, 1970). The medial and lateral posterior ciliary arteries supply the optic nerve head, the outer retina, and, in 20 to 50% of individuals, a variable area of inner retina contiguous with the optic disc (Hayreh, 1969); the central retinal artery supplies the remainder of the inner retina.

We present a patient with a unique combination of fundus signs resulting from arteritic obstruction of the blood supply to each of the above arterial territories. The clinical findings are correlated with recent experimental work on the pathophysiology of ischaemic fundus lesions.

Case report

A 75-year-old woman presented with a 2-week history of 'misty' vision in each eye. She had suffered weight loss, bitemporal headaches, jaw claudication, and aching limbs during the previous 3 months.

On examination vision in each eye was found to be reduced to perception of hand movements only. Pupil reactions were sluggish, and there was a left relative afferent pupillary defect. Examination of the right fundus revealed pallor and swelling of the optic disc and mild translucent swelling of the temporal parapapillary retina (Fig. 1). The ischaemic retina was supplied by two small cilioretinal arterioles and was delineated temporally by a discrete border zone of opaque swelling of the nerve fibre layer (cotton-wool spots). The central arterioles showed irregular narrowing consistent with age, and the central venous tributaries were of normal calibre and colour. No abnormality of the inner retina was noted in the territory of supply of the central retinal artery.

At first sight the left eye showed a similar ophthalmoscopic picture, with pale swelling of the nasal part of the optic disc and a row of fluffy white cotton-wool spots crossing the papillomacular bundle (Fig. 2). However, there was no cilioretinal arteriolar supply to this eye, and the temporal parapapillary retina was normal in appearance. The remainder of the fundus showed diffuse translucent swelling of the inner retina sparing the fovea, and a band of opacity of the outer retina was noted in the macula (Fig. 2). The central arterioles were attenuated, and the venous blood was markedly deoxygenated.

Fluorescein fundus angiography on the right showed satisfactory filling of the central retinal artery but slow filling of the choroid, optic nerve head, and cilioretinal arterioles. In the left eye markedly impaired perfusion was evident in the territories of supply of both the posterior ciliary arteries and the central retinal artery. Both optic discs showed excessive dye leakage in the late pictures. The right eye had a normal electroretinogram (ERG) and electro-oculogram (EOG), but there were minimal electroretinal responses from the left eye.

The patient appeared to be indifferent to her loss of sight. No other abnormality was found on general examination. The erythrocyte sedimentation rate (ESR) was raised at 116 mm in the first hour. The temporal arteries were palpable but non-pulsatile, and biopsy of the right superficial temporal artery showed inflammatory cell infiltration and thickening of the vessel wall with giant cells, thus confirming the clinical diagnosis of temporal arteritis.

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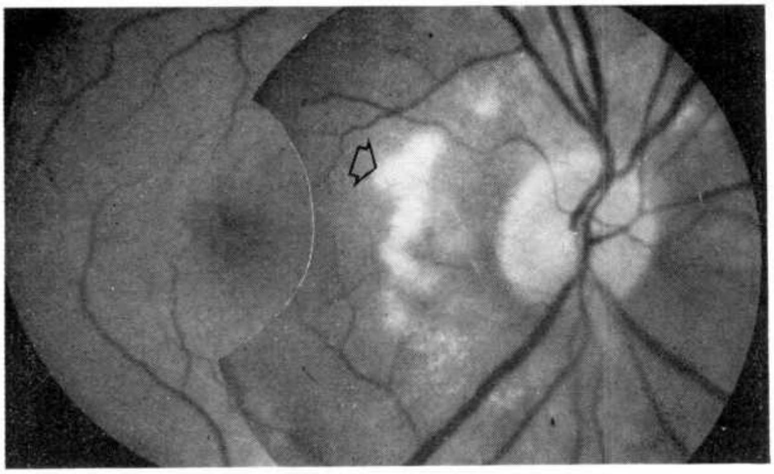

Fig. 1 *Composite fundus photograph of right eye on presentation. Cotton-wool spots* (open arrow) *delineate temporal border of ischaemic cilioretinal arteriolar territory. Nasal part of optic disc is swollen*

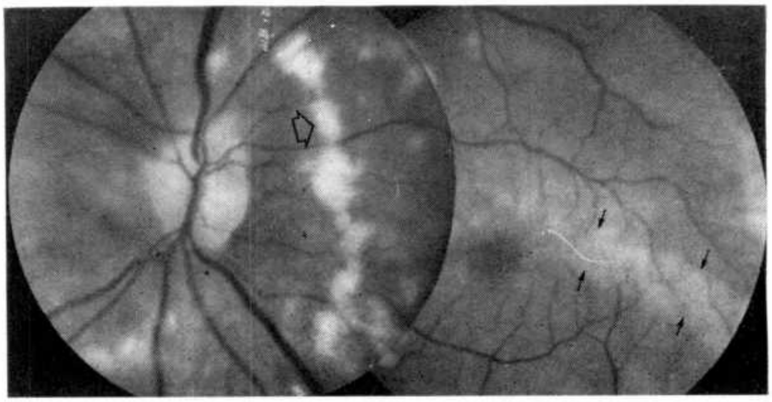

Fig. 2 *Composite fundus photograph of left eye on presentation. Cotton-wool spots* (open arrow) *delineate ischaemic temporal retina. Nasal part of optic disc is swollen. Outer retinal infarction inferotemporal to fovea* (fine arrows)

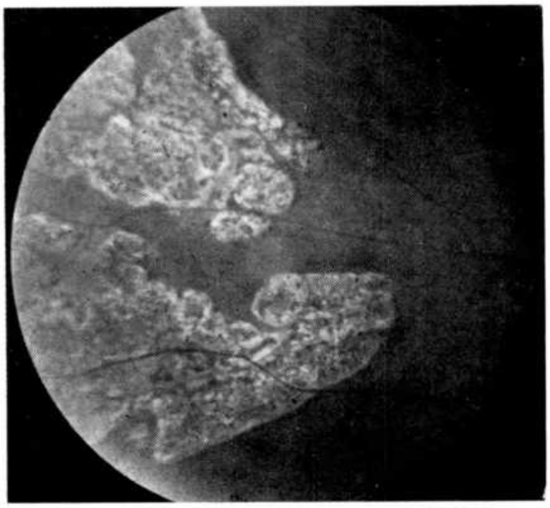

Fig. 3 *Fundus photograph of nasal retina of left eye 1 month after presentation. Pigmented lesions of outer retina in territory of medial posterior ciliary artery*

Treatment with systemic steroids was instituted immediately. The patient initially received 90 mg of prednisolone daily, and this was gradually reduced as the ESR became normal. A month after she was first seen her vision in the right eye had improved to 6/9 and in the left eye to 6/36. However, the fields of vision were grossly restricted, both eyes showing complete inferior altitudinal defects. The optic discs were pale but not cupped, and the retinal nerve fibre bundle striations were absent, indicating loss of neurones. In the left eye wedge-shaped areas of pigment epithelial disturbance were noted nasal to the optic disc (Fig. 3), and bands of pigmentary change (Siegrist streaks) were also present inferotemporal to the fovea where outer retinal infarction had been seen on presentation. The left relative afferent pupillary defect persisted.

Discussion

Ischaemic optic neuropathy, as seen in the right eye of our patient, is the commonest ocular presentation

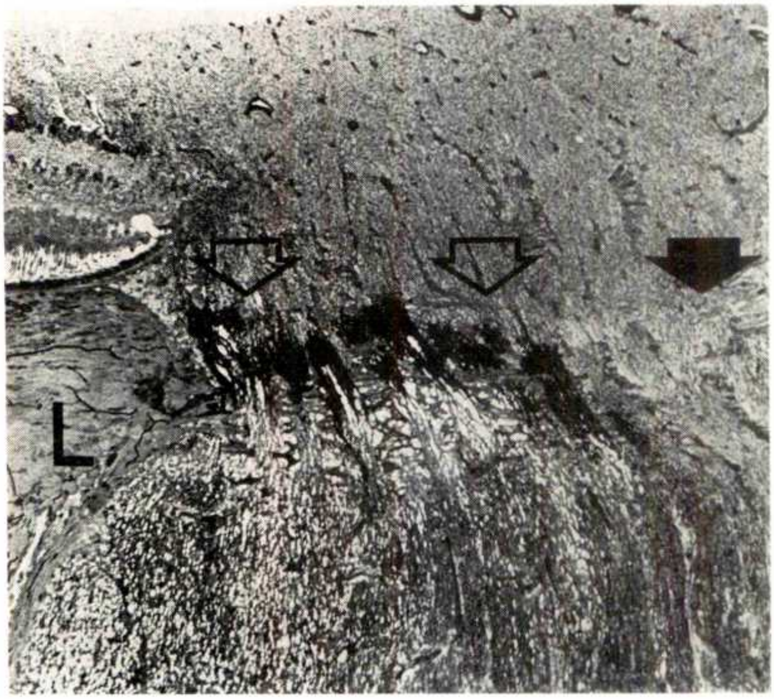

Fig. 4 *Autoradiograph of horizontal section through the optic nerve head of a monkey. The lateral posterior ciliary artery was occluded and* ^{3}*H-leucine was then injected intravitreally and left for 5 hours before enucleation. Ischaemic vacuolation in laminar* (L) *and retrolaminar regions temporally. Intra-axonal accumulation of label in prelaminar region temporally* (open arrows). *Label transported normally into nasal part of optic nerve* (solid arrow)

of temporal arteritis and results from involvement of the posterior ciliary circulation in the arteritic process (Foulds, 1969; Hayreh, 1969). Experimental occlusion of the posterior ciliary arteries in monkeys resulted in similar disc swelling (Hayreh and Baines, 1972a), but no definitive histological investigation of the acute disc lesion was carried out. Our recent investigation (McLeod *et al.*, 1978) has substantiated the hypothesis (McLeod, 1975, 1976; Hayreh, 1977) that the disc swelling results from interruption of orthograde axoplasmic transport in retinal ganglion cell axons (Figs. 4 and 5).

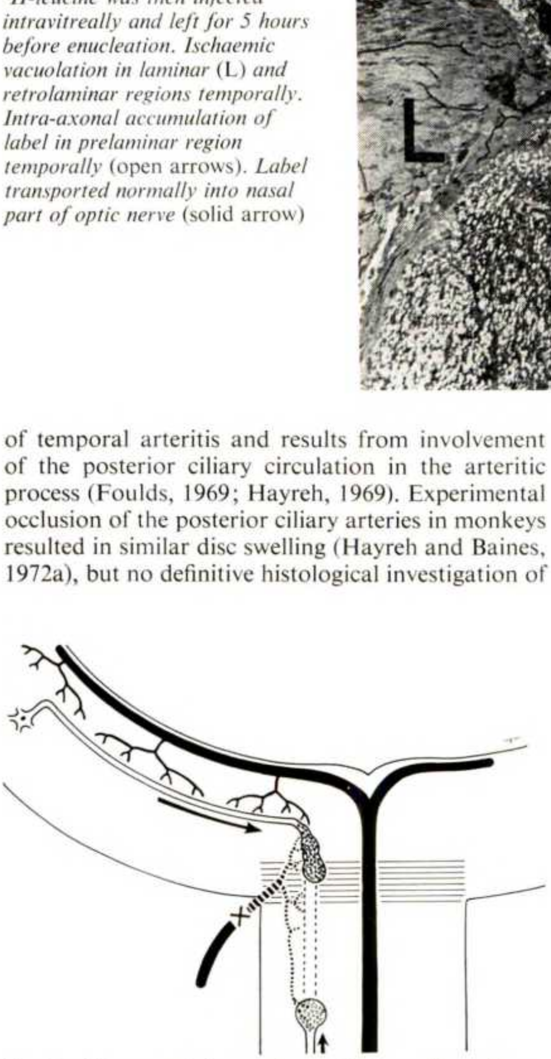

Fig. 5 *Diagram of changes in a retinal ganglion cell axon after occlusion* (X) *of posterior ciliary artery. Ischaemic vacuolation in optic nerve head* (axolemma dotted). *Axonal swellings from obstructed orthograde* (long arrow) *and retrograde* (short arrow) *axoplasmic transport*

In our patient's right eye occlusion of the posterior ciliary arteries also resulted in parapapillary infarction of the inner retina. The cotton-wool spots which delineated the temporal border of the cilioretinal infarct can also be attributed to obstruction of orthograde axoplasmic transport in the retinal nerve fibre layer (McLeod, 1975). Such an accumulation of axoplasm has been demonstrated in autoradiographic studies of retinal infarcts in pigs (McLeod *et al.*, 1977).

The cotton-wool spots in our patient's left eye delineated the nasal border of a large infarct of the inner retina which resulted from partial occlusion of the central retinal artery (Oji and McLeod, 1978). This accumulation of axoplasmic debris corresponds to that seen on the disc side of retinal infarcts produced experimentally (McLeod *et al.*, 1977) and reflects obstruction of retrograde axoplasmic transport in the retina. The band and wedge-shaped infarcts of the *outer* retina resulted from arteritic involvement of the posterior ciliary arterial supply to the left eye. Although such infarcts are readily produced by occlusion of the posterior ciliary arteries in monkeys (Hayreh and Baines, 1972b), they are relatively unusual in temporal arteritis, probably owing to incomplete occlusion of the posterior ciliary supply and some capacity of the inner retinal circulation to sustain outer retinal viability during choroidal ischaemia. It is therefore of interest that in our patient, and also in a case previously illustrated (McLeod, 1973), outer retinal infarcts developed in eyes with combined involvement of the central retinal and posterior ciliary circulations.

Finally, the improvement in central vision which followed treatment of our patient with systemic steroids illustrates the remarkable ability of neurones to survive prolonged ischaemia. Recovery of central vision despite infarction of the papillomacular bundle has previously been noted in cases of cilioretinal infarction (McLeod and Ring, 1976) and probably reflects the survival of axons on the vitreal aspect of the retinal nerve fibre layer.

Mr Lorimer Fison kindly allowed us to report on his patient. Messrs K. Sehmi, T. Tarrant, and P. L. Ansell assisted with the illustrations, and Miss Heather Lucas and Miss L. Martin prepared the manuscript.

References

Foulds, W. S. (1969). Visual disturbances in systemic disorders, optic neuropathy and systemic disease. *Transactions of the Ophthalmological Societies of the United Kingdom*, **89**, 125–146.

Hayreh, S. S. (1969). Blood supply of the optic nerve-head and its role in optic atrophy, glaucoma and oedema of the optic disc. *British Journal of Ophthalmology*, **53**, 721–748.

Hayreh, S. S. (1977). Optic disc oedema in raised intracranial pressure: V. Pathogenesis. *Archives of Ophthalmology*, **95**, 1553–1565.

Hayreh, S. S., and Baines, J. A. B. (1972a). Occulsion of the posterior ciliary artery: III. Effects on the optic nerve-head. *British Journal of Ophthalmology*, **56**, 754–764.

Hayreh, S. S., and Baines, J. A. B. (1972b). Occlusion of the posterior ciliary artery: II. Chorio-retinal lesions. *British Journal of Ophthalmology*, **56**, 736–753.

Henkind, P., Charles, N. S., and Pearson, J. (1970). Histopathology of ischemic optic neuropathy. *American Journal of Ophthalmology*, **69**, 78–90.

McLeod, D. (1973). Electroretinal responses in ocular vascular occlusions due to temporal arteritis. *British Journal of Ophthalmology*, **57**, 921–934.

McLeod, D. (1975). Clinical signs of obstructed axoplasmic transport. *Lancet*, **2**, 954–956.

McLeod, D. (1976). Ophthalmoscopic signs of obstructed axoplasmic transport after ocular vascular occlusions. *British Journal of Ophthalmology*, **60**, 551–556.

McLeod, D., Marshall, J., Kohner, E. M., and Bird, A. C. (1977). The role of axoplasmic transport in the pathogenesis of retinal cotton-wool spots. *British Journal of Ophthalmology*, **61**, 177–191.

McLeod, D., Marshall, J., and Kohner, E. M. (1978). Pathogenesis of Ischaemic Disc Swelling. *Journal of Clinical Science and Molecular Medicine*, **54**, 31.

McLeod, D., and Ring, C. P. (1976). Cilioretinal infarction after retinal vein occlusion. *British Journal of Ophthalmology*, **60**, 419–427.

Oji, E., and McLeod, D. (1978). Partial central retinal artery occlusion. *Transactions of the Ophthalmological Societies of the United Kingdom*, **98**. (In press.)

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Macular abnormalities in the reattached retina

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SUMMARY Sixty-six patients in whom the macula was detached before surgery were observed for at least 1 year after retinal reattachment. Macular abnormalities were recognised clinically in most patients with severely reduced vision. Failure of retinal receptor regeneration or receptor misalignment may account for visual reduction in a minority of patients but may be less important as a cause of reduced visual acuity than was previously supposed. This study confirms that the visual prognosis is related to the duration of the detachment before surgery, and patients with a macular detachment for 2 months or longer are likely to suffer persistently reduced vision.

Visual recovery is frequently incomplete after surgical reattachment of the retina. The visual acuity after successful reattachment has been documented by several workers (Jay, 1965; Hudson, 1968; Gundry and Davies, 1974; Grupposo, 1975), but the precise causes of reduced vision in the patients studied were not identified. The recovery of visual acuity for up to 2 years after retinal reattachment and the improvement in hue discrimination for as long as 4 years have been attributed to regeneration of retinal receptor outer segments (Foulds and Ikeda, 1966; Chisholm *et al.*, 1973; Gundry and Davies, 1974). Such regeneration has been demonstrated in the owl and rhesus monkey after repositioning of experimentally induced retinal detachments (Machemer, 1968b; Kroll and Machemer, 1969). Conversely, a failure of visual recovery has been accounted for by incomplete receptor regeneration or by receptor misalignment (Machemer, 1968b; Aaberg and Machemer, 1970; Enoch *et al.*, 1973). It is acknowledged that the visual outcome after successful retinal detachment surgery may also be prejudiced by the presence of cystoid degeneration at the macula (Reese, 1937), pigment epithelial changes at the macula (Reese, 1937; Hudson, 1968), macular pucker (Hudson, 1968; Tanenbaum and Schepens, 1969; Gundry and Davies, 1974), or macular oedema (Ryan, 1973), although the precise incidence of detectable macular abnormalities in the reattached retina is unknown. We undertook this study to document the morphological abnormalities observed clinically at the macula after surgical reattachment of the retina in an attempt to assess the importance of detectable macular abnormalities at the macula relative to recovery of visual acuity.

Patients and methods

A total of 75 patients were entered in this study, but 3 were withdrawn because of increasing lens opacities and 6 failed to attend for follow-up examination. We are reporting on 66 who had been observed for at least 1 year. Consecutive patients were selected in whom the macula was detached preoperatively and reattached postoperatively. Patients were excluded when there was a recognised pre-existing macular disease, opacities in the ocular media, giant retinal tears, and when silicone oil injection had been used to flatten the retina.

Examinations were carried out at intervals of 2 weeks, 4 weeks, 3 months, 6 months, 1 year, and 2 years after surgery. At each examination, the following assessments were made: corrected visual acuity, biomicroscopy of the anterior segment and vitreous, fundus examination by binocular indirect ophthalmoscopy, and a detailed clinical examination of the macula using the Hruby lens. The appearance of the macula was recorded by stereoscopic colour photography and fluorescein fundus angiography at each visit.

Results

VISUAL ACUITIES

At 1 year after surgery the visual acuity had improved in 54 (82%) patients, remained the same in 7 (11%), and worsened in 5 (7%) (Fig. 1). A visual acuity of 6/60 or less was recorded in 47 patients

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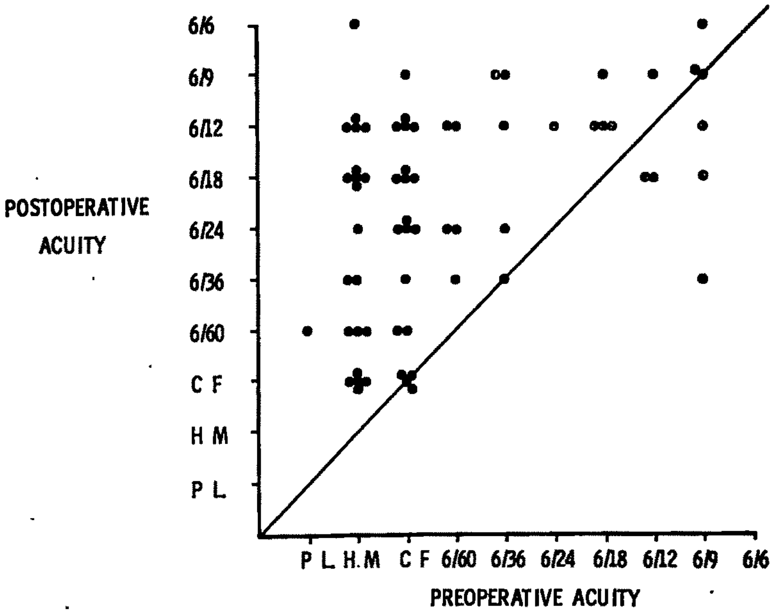
(71%) preoperatively but in only 15 patients (22%) at one year after surgery. At 1 year 25 patients (37%) had recovered to a visual acuity of 6/12 or better, but only 2 patients had a visual acuity of 6/6 (Fig. 2).

MORPHOLOGICAL APPEARANCES

The macula appeared normal, both on clinical examination and on fluorescein angiography, in 16 patients. Only 3 patients with a normal macular appearance had a visual acuity of less than 6/12 (Fig. 3). In 1 of these amblyopia was suspected; in another, a high myope, the best vision in the unoperated eye was 6/18; and the 1 other patient had a normal macular appearance with a visual acuity of 6/24 which was unexplained.

A disturbance of the surface reflex at the macula with or without recognisable preretinal fibrous tissue, but not associated with distortion of the retinal vessels (cellophane maculopathy), was observed in 6 patients (Fig. 4*a*). The visual acuity was 6/12 or better in 4 of these and 6/18 in the

Fig. 1 *Scattergram showing change in visual acuity in 66 eyes 1 year after retinal reattachment (PL = perception of light. HM = hand movements. CF = counting fingers)*



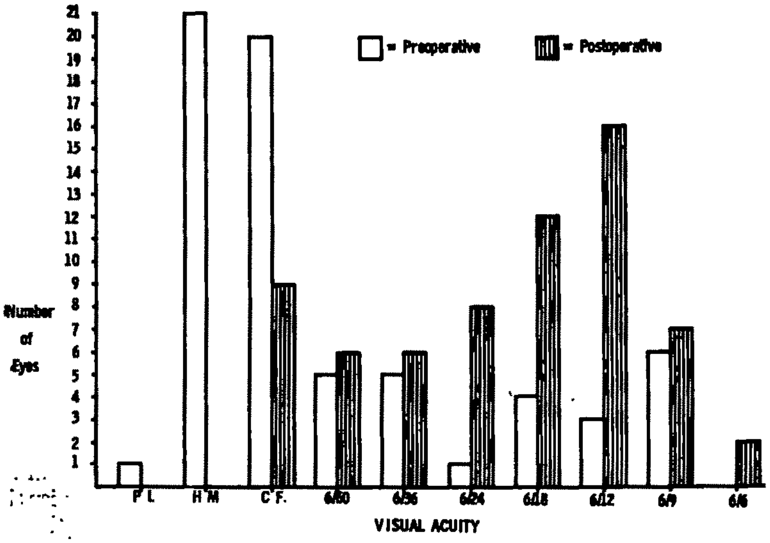


Fig. 2 *Histogram showing the change in distribution of visual acuity in 66 eyes 1 year after retinal reattachment*

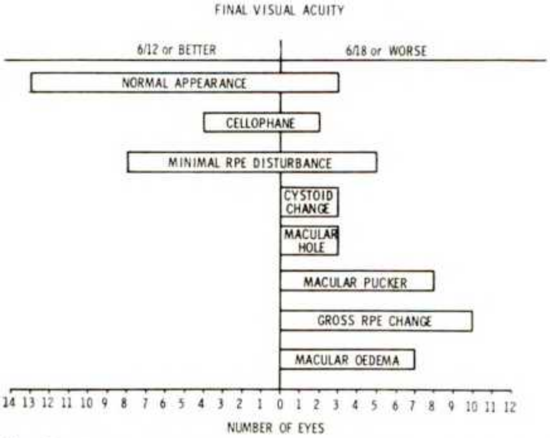


Fig. 3 *Bar chart showing the relationship between the morphological appearance of the macula and the visual acuity in 66 eyes 1 year after retinal reattachment (RPE = retinal pigment epithelium)*

other 2 (Fig. 3). More severe preretinal fibrosis with opaque fibrous tissue at the macula and distortion of the retina and traction on the surrounding retinal vessels (macular pucker) occurred in 8 patients and was associated with a visual acuity of 6/36 or less in all (Figs. 3 and 4*b*). Fluorescein angiography showed the marked distortion of the retinal blood vessels at the macula and the accompanying dye leakage.

Minimal disturbance in the retinal pigment epithelium at the macula was diagnosed and confirmed by fluorescein angiography in 13 patients. Of these, 8 had a visual acuity of 6/12 or better, 3 had a visual acuity of 6/18, and 2 had a visual acuity of 6/24 (Fig. 3). Gross disturbance in the retinal pigment epithelium at the macula occurred in 10 patients. In 4 of these, pigment epithelial abnormalities followed the resolution of intraretinal cystoid changes (Fig. 5). One patient had a visual acuity of 6/24, and all the other patients had a visual acuity of 6/36 or worse (Fig. 3).

Cystoid changes were visible at the macula in the early studies of 7 patients, all of whom were phakic. The intraretinal cystoid spaces were seen on biomicroscopic examination and colour photographs, but the angiographic appearance of the macula was unremarkable (Figs. 5 and 6). However, at 6 months after surgery 4 of these patients had gross disturbance of the retinal pigment epithelium at the macula and the cystoid spaces were no longer visible (Fig. 5). The 3 patients with persistent cystoid changes had visual acuities of 6/18, 6/24, and 6/36.

Macular oedema characterised by intraretinal accumulation of dye during fluorescein angiography occurred in a total of 17 patients (Figs. 7 and 8). Persistent oedema was associated with a visual acuity of 6/18 or worse (Fig. 7). In 2 aphakic patients the oedema resolved in one and persisted in the other. Ten patients had macular oedema at 9 months after surgery, and in 7 it was still present at 18 months (Fig. 9).

A full-thickness macular hole was seen after retinal reattachment in 3 patients, and all 3 patients had a visual acuity of 6/60. Fluorescein angiography showed the typical central transmission defects.

Pigment fallout was observed at the macula in 7 patients. Four had a visual acuity of 6/12 or better. The macula was otherwise normal in 2 of

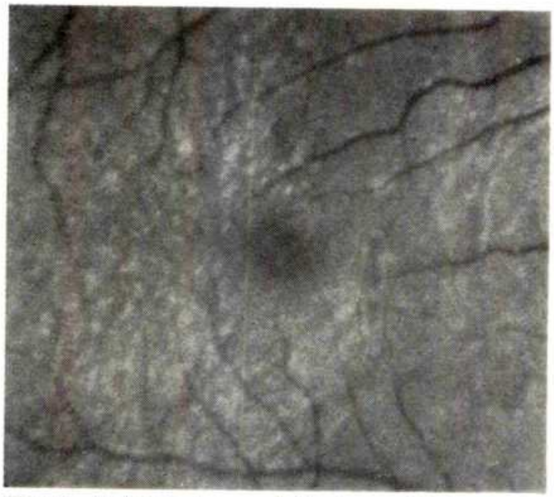


Fig. 4a *Red-free photograph showing a mild degree of preretinal fibrosis at the macula (cellophane maculopathy)*

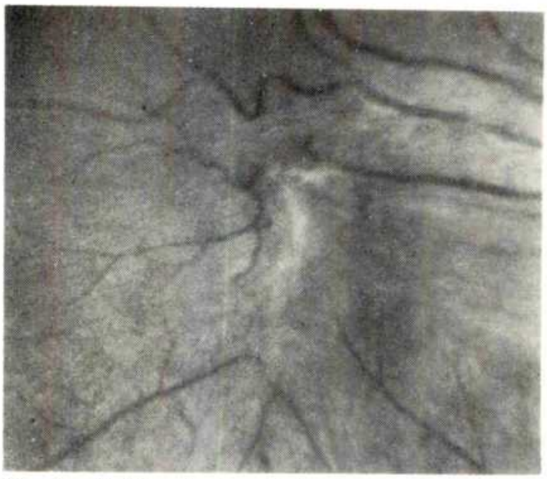


Fig. 4b *Red-free photograph showing macular pucker*

these. One patient had a minor disturbance in the retinal pigment epithelium and one had a cellophane maculopathy. The 3 other patients with pigment fallout had a visual acuity of 6/36 or worse, and all had other changes at the macula—either macular pucker, a gross disturbance in the retinal pigment epithelium, or persistent macular oedema.

DURATION OF RETINAL DETACHMENT

The duration of retinal detachment varied from less than 1 week in some patients to more than 2 years in others (Fig. 10). After a retinal detachment of 1 month's duration or less the macula was usually normal or showed pucker, oedema, or minimal retinal pigment epithelial changes. However, a retinal detachment of 2 months' duration or longer was followed by gross retinal pigment epithelial changes at the macula in 8 out of 16 patients (50%) in this series (Fig. 10).

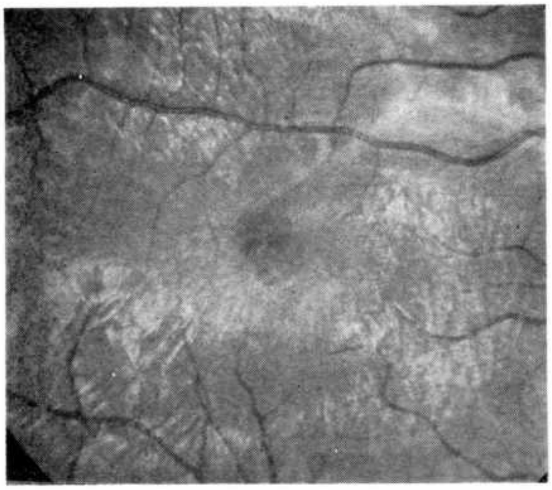


Fig. 5a *Red-free photograph showing intraretinal cystoid spaces at the macula 3 months after reattachment. The high watermark of the detachment is visible running obliquely above the superior temporal vessels*

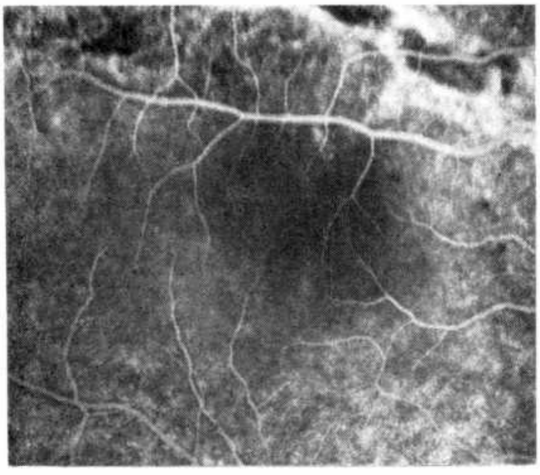


Fig. 5b *The fluorescein angiogram at 3 months showing no leakage of dye from perifoveal retinal capillaries. The high watermark is clearly visible*

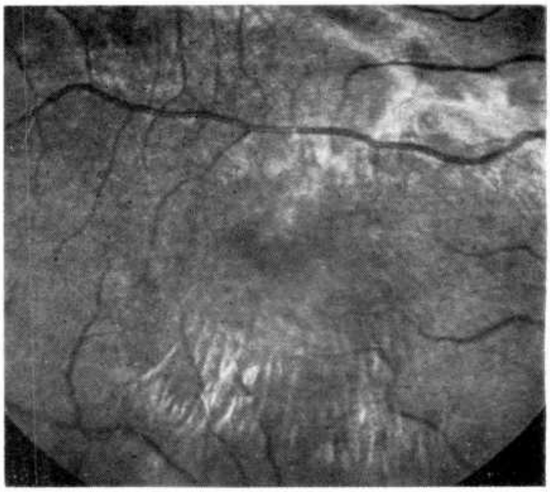


Fig. 5c *Red-free photograph 9 months after retinal reattachment. The intraretinal cystoid spaces are no longer visible, but there are retinal pigment epithelial changes at the macula*

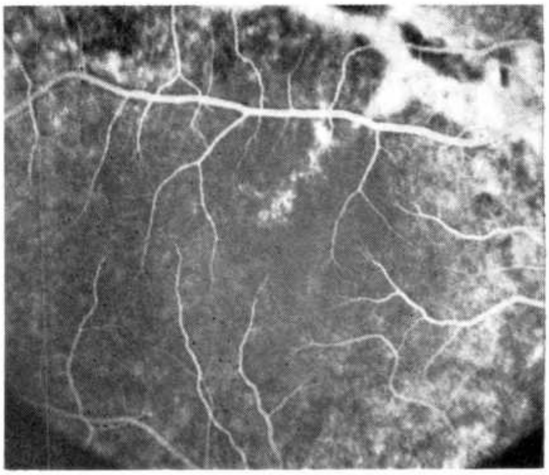


Fig. 5d *The fluorescein angiogram now shows transmission defects corresponding with the retinal pigment epithelial changes*

TYPE OF SURGICAL PROCEDURE

All eyes were treated by scleral buckling and cryopexy through full-thickness sclera. Local Silastic sponge explants were used in 55 and encircling silicone-rubber bands in 11. In 27 eyes the subretinal fluid was drained, while in 39 it was left to absorb spontaneously.

Of 14 eyes in which preretinal fibrosis occurred at the macula after surgery 9 had local explants and 5 had encircling bands; 8 were drained and 6 were not. In 17 eyes with macular oedema there were 10 local explants and 7 encircling bands; 10 were drained and 7 were not.

Discussion

Macular abnormalities were identified in the majority of patients with severely reduced vision after retinal reattachment. Abnormalities such as cystoid degeneration at the macula, macular hole, macular pucker, a gross retinal pigment epithelial disturbance, or macular oedema appeared easily sufficient to account for a low visual acuity (Fig. 3). However, persistently reduced vision could not be attributed to macular changes in every case. A minority of patients had either a normal macula, cellophane maculopathy, or a minimal disturbance of the retinal pigment epithelium, with low visual acuity, and it is conceivable that visual reduction in these patients is the result of an abnormality or failure of retinal receptor regeneration. Indeed, abnormal or incomplete retinal receptor regeneration may explain why so few patients in this series achieved a visual acuity of 6/6 (Fig. 2).

In the clinical examination of the macula we found the magnification offered by slit-lamp biomicroscopy as opposed to indirect ophthalmoscopy particularly useful. Fluorescein angiography was also helpful in distinguishing macular oedema from cystoid degeneration, in demonstrating macular pucker, and in confirming the presence of macular hole or retinal pigment epithelial disturbance.

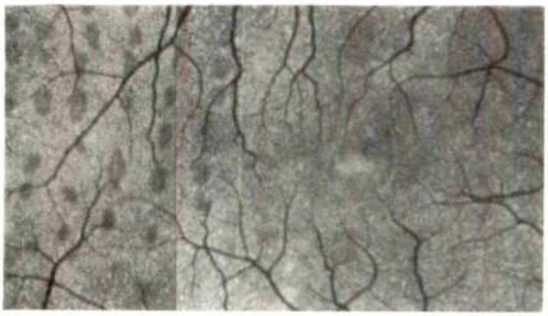


Fig. 6a *Red-free photographs at 3 months showing thickened retina and intraretinal cystoid spaces at the macula. Temporal to the macula are multiple round lesions, probably at the level of the retinal pigment epithelium, which may represent resolution of small localised serous retinal detachments*

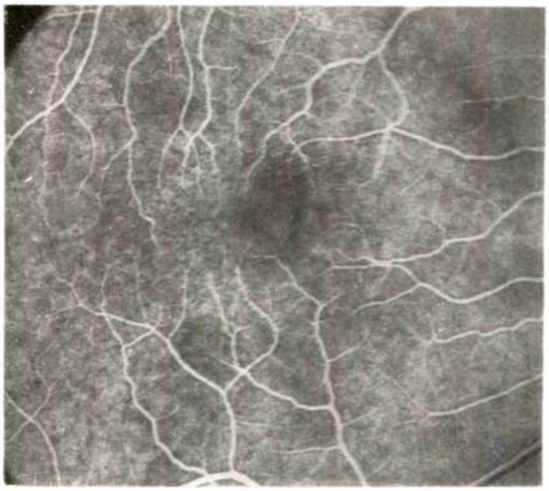


Fig. 6b *Fluorescein angiogram shows no leakage from perifoveal retinal capillaries. The multiple round lesions show faintly as masking the background choroidal fluorescence*

Preretinal fibrous tissue at the macula was the most frequently recognised abnormality. It is acknowledged as a common cause of poor vision after successful retinal detachment surgery (Gass, 1972; Gundry and Davies, 1974), varying from a mild disturbance of the surface reflex from the retina (cellophane maculopathy), with minimal visual loss, to severe retinal distortion (macular pucker), with profound loss of central vision. The pathogenesis of preretinal fibrosis is complex (Foos, 1974; Gloor and Daicker, 1975; Bellhorn *et al.*, 1975; Machemer and Laqua, 1975), but in this study it was apparently unrelated to the type, extent, or duration of the retinal detachment, or to the type of surgical procedure used to reattach the retina.

Pigmentary changes in the reattached retina can be attributed to degeneration and loss of retinal pigment epithelial cells (Hogan and Zimmerman, 1962; Machemer, 1968a). Typically, gross disturbance of the retinal pigment epithelium followed long-standing retinal detachments, where atrophy of the retinal receptor layer could also have accounted for poor vision (Hogan and Zimmerman, 1962; Aaberg and Machemer, 1970). Pigmentary changes have also been attributed to choroidal infarction as a result of scleral buckling (Foulds *et al.*, 1971), and in this study a single patient had

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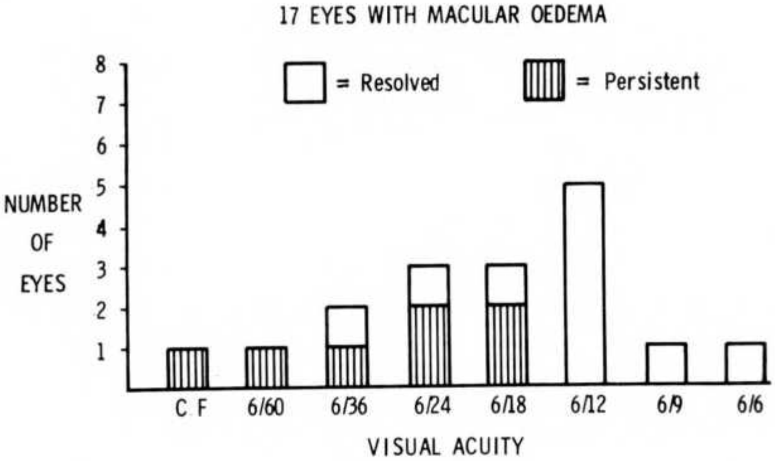

Fig. 7 *Histogram showing visual outcome at 1 year after retinal reattachment in 17 eyes with macular oedema*

grossly delayed choroidal perfusion on fluorescein angiography which corresponded with an area of retinal pigment epithelial disturbance involving the macula. However, no other patient had impaired choroidal perfusion in the macular or paramacular areas, although this does not exclude ischaemic episodes at the time of surgery.

Cystoid macular oedema characterised by leakage from retinal vessels has been recognised as a cause of reduced vision after retinal detachment surgery in both aphakic and phakic eyes (Ryan, 1973). This finding was supported by our observation that persistent macular oedema was associated with a visual acuity of 6/18 or worse, and resolution of oedema was accompanied by an improvement in visual acuity (Fig. 7). Macular oedema was less common than after cataract extraction, but its course was more prolonged and it persisted more often (Hitchings *et al.*, 1975; Meredith *et al.*, 1976). The presence of oedema did not correlate with the age of the patient, with the apparent degree of intraocular inflammation, or with the type of surgical procedure used to reattach the retina.

We have distinguished between cystoid degeneration, without leakage from retinal vessels on fluorescein angiography, and cystoid macular oedema. Typically, cystoid degeneration occurs after longstanding retinal detachments. It may be accompanied by loss of neural tissue in the retina and atrophy of the receptors (Hogan and Zimmerman, 1962;

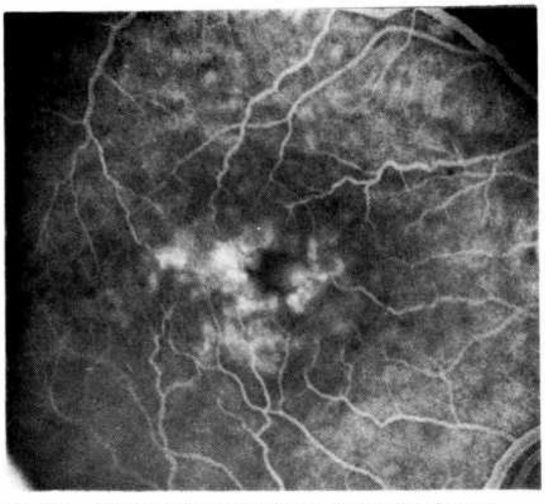

Fig. 8a *Fluorescein angiogram at 6 months showing macular oedema*

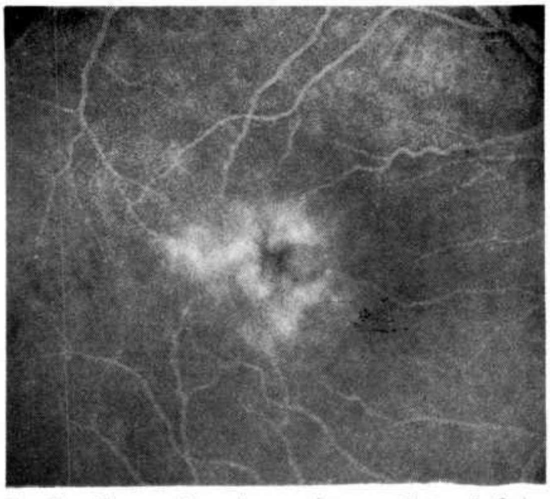

Fig. 8b *Fluorescein angiogram (same patient as in 8a) at 15 months showing persistence of macular oedema*

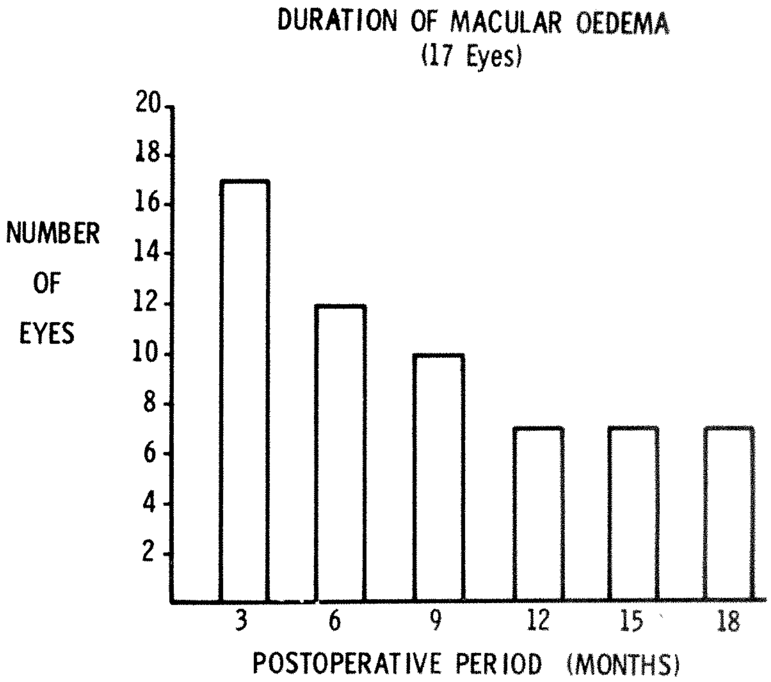

Fig. 9 *Histogram showing the duration of macular oedema in 17 eyes up to 18 months after retinal reattachment*

Machemer, 1968a), which could certainly account for persistently reduced vision. When the cystoid degeneration resolved, it was often followed by retinal pigment epithelial changes at the macula as noted previously (Reese, 1937), but the visual acuity did not improve. The development of these cystoid changes, which are unrelated to retinal capillary permeability, may be the result of a metabolic abnormality in the detached retina (Aaberg and Machemer, 1970) and may resemble the cystoid degeneration seen at the macula in patients with juvenile X-linked retinoschisis (Deutman, 1971)

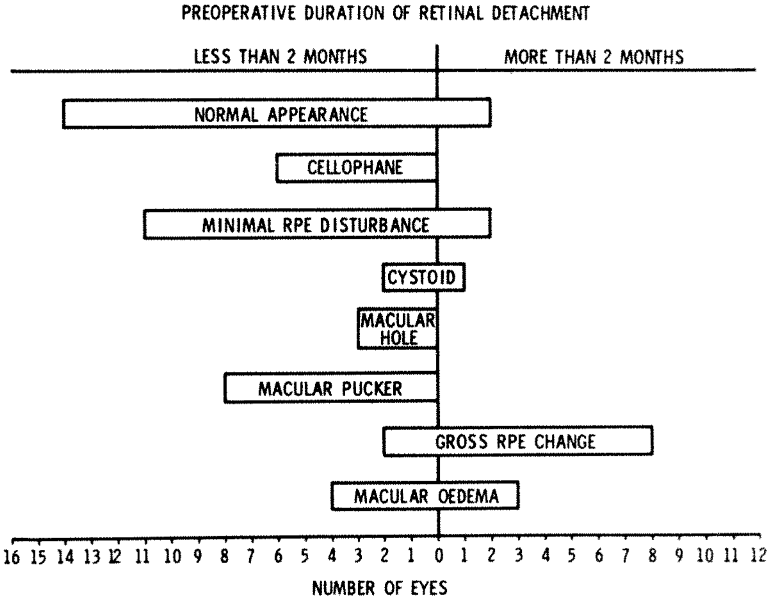

Fig. 10 *Bar chart showing the relationship between the morphological appearance at the macula 1 year after surgery and the preoperative duration of retinal detachment*

and in some patients with retinitis pigmentosa (Gass, 1970; ffytche, 1972; Fishman *et al.*, 1977) and in nicotinic acid maculopathy (Gass, 1973).

Reduced vision after retinal reattachment has also been attributed to subretinal pigment migration and accumulation at the macula as a result of cryotherapy (Shea, 1968; Abraham and Shea, 1969; Sudarsky and Yanuzzi, 1970). We observed 3 patients with pigment fallout at the macula and reduced vision, but all 3 had other macular abnormalities which were certainly sufficient to account for a low visual acuity. By contrast the 4 patients with only pigment fallout at the macula had good vision, supporting the assertion that subretinal pigment migration does not of itself result in visual loss or diminished retinal sensitivity (Hilton, 1974).

After surgical reattachment of experimentally induced retinal detachments in owl monkeys multiple small localised retinal detachments were demonstrated by fluorescein angiography and by histopathology (Machemer, 1968b). Such small localised detachments have not been documented in human eyes and were not identified in this series. However, a single patient showed an appearance suggestive of small localised serous detachments of the retina which had resolved and no longer filled with dye on the fluorescein angiogram (Fig. 5).

The results in this study suggest that severely reduced vision after retinal reattachment may be accounted for by morphological abnormalities at the macula which are easily recognised by slit-lamp biomicroscopy. It is confirmed that the visual prognosis is related to the duration of the detachment before surgery and that patients with a macular detachment for 2 months or longer are likely to suffer persistently reduced vision. Cystoid degeneration and gross retinal pigment epithelial changes follow long-standing retinal detachments and are largely predictable. However, macular pucker as a result of preretinal fibrosis and cystoid macular oedema due to leakage from retinal capillaries emerge as serious and unpredictable causes of severely reduced vision after retinal reattachment. Both conditions are responsible for low vision after a wide range of ophthalmic surgical procedures, their pathogenesis is ill understood, and at present both are difficult to treat. The prevention or successful treatment of these 2 complications could alter radically the visual prognosis for retinal detachment surgery.

We wish to thank Mr A. C. Bird and Mr L. G. Fison for their helpful advice and encouragement during this study. We are grateful to Mr K. S. Sehmi and Mr T. Tarrant of the Audiovisual Department, Institute of Ophthalmology, Judd Street, London WC1, for preparing the illustrations and to Miss H. Lucas for secretarial assistance.

References

Aaberg, T. M., and Machemer, R. (1970). Correlation of naturally occurring detachments with long-term retinal detachment in the owl monkey. *American Journal of Ophthalmology*, **69**, 640–650.

Abraham, R. K., and Shea, M. (1969). Significance of pigment dispersion following cryoretinopexy: scotomata and atrophy. *Modern Problems in Ophthalmology*. Vol. 8, pp. 455–461. S. Karger: Basel.

Bellhorn, M. B., Friedman, A. H., Wise, G. N., and Henkind, P. (1975). Ultrastructure and clinicopathologic correlation of idiopathic preretinal macular fibrosis. *American Journal of Ophthalmology*, **79**, 366–373.

Chisholm, I. A., McClure, E., and Foulds, W. S. (1973). Functional recovery of the retina after retinal detachment. *Transactions of the Ophthalmological Societies of the United Kingdom*, **95**, 167–172.

Deutman, A. F. (1971). *The Hereditary Dystrophies of the Posterior Pole of the Eye*, p. 52. Van Gorcum Assen: Netherlands.

Enoch, J. M., Van Lee, J. A., and Okun, E. (1973). Realignment of photoreceptors disturbed in orientation secondary to retinal detachment. *Investigative Ophthalmology*, **12**, 849–853.

ffytche, T. J. (1972). Cystoid maculopathy in retinitis pigmentosa. *Transactions of the Ophthalmological Societies of the United Kingdom*, **92**, 265–283.

Fishman, G. A., Maggiano, J. M., and Fishman, M. (1977). Foveal lesions seen in retinitis pigmentosa. *Archives of Ophthalmology*, **95**, 1993–1996.

Foos, R. Y. (1974). Vitreoretinal juncture—simple epiretinal membranes. *Albrecht von Graefes Archiv für klinische und experimentelle Ophthalmologie*, **189**, 231–250.

Foulds, W. S., and Ikeda, H. (1966). The effects of detachment of the retina on the induced and resting ocular potentials in the rabbit. *Investigative Ophthalmology*, **5**, 93–108.

Foulds, W. S., Lee, W. R., and Taylor, W. O. G. (1971). Clinical and pathological aspects of choroidal ischaemia. *Transactions of the Ophthalmolological Societies of the United Kingdom*, **91**, 323–341.

Gass, J. D. M. (1970). *Stereoscopic Atlas of Macular Disease*, 1st edn., p. 154. C. V. Mosby: St. Louis.

Gass, J. D. M. (1972). *Retina Congress*, pp. 195–198. Appleton-Century-Crofts: New York.

Gass, J. D. M. (1973). Nicotinic acid maculopathy. *American Journal of Ophthalmology*, **76**, 500–510.

Gloor, P. G., and Daicker, B. C. (1975). Pathology of the vitreo-retinal border structures. *Transactions of the Ophthalmological Societies of the United Kingdom*, **95**, 387–390.

Grupposo, S. S. (1975). Visual acuity following surgery for retinal detachment. *Archives of Ophthalmology*, **93**, 327–330.

Gundry, M. S., and Davies, E. W. G. (1974). Recovery of vision after retinal detachment surgery. *American Journal of Ophthalmology*, **77**, 310–314.

Hilton, G. F. (1974). Subretinal pigment migration. *Archives of Ophthalmology*, **91**, 445–450.

Hitchings, R. A., Chisholm, I. H., and Bird, A. C. (1975). Aphakic macular oedema: incidence and pathogenesis. *Investigative Ophthalmology*, **14**, 68–72.

Hogan, M. J., and Zimmerman, L. E. (1962). *Ophthalmic Pathology*, p. 562. W. B. Saunders: New York.

Hudson, J. H. (1968). *New and Controversial Aspects of Retinal Detachment*, pp. 460–467. Hoeber: New York.

Jay, B. (1965). The functional cure of retinal detachments. *Transactions of the Ophthalmological Societies of the United Kingdom*, **85**, 101–110.

Kroll, A. J., and Machemer, R. (1969). Experimental retinal detachment in the owl monkey: (v) Electron microscopy of the reattached retina. *American Journal of Ophthalmology*, **67**, 117–130.

Machemer, R. (1968a). Experimental retinal detachment in the owl monkey: (ii) Histology of retina and pigment epithelium. *American Journal of Ophthalmology*, **66**, 396–410.

Machemer, R. (1968b). Experimental retinal detachment in the owl monkey: (iv) The reattached retina. *American Journal of Ophthalmology*, **66**, 1075–1091.

Machemer, R., and Laqua, H. (1975). Pigment epithelium proliferation in retinal detachment. *American Journal of Ophthalmology*, **80**, 1–23.

Meredith, T. A., Kenyon, K. R., Singerman, L. J., and Fine, S. L. (1976). Perifoveal vascular leakage and macular oedema after intracapsular cataract extraction. *British Journal of Ophthalmology*, **60**, 765–769.

Reese, A. B. (1937). Defective central vision following successful operation for detachment of the retina. *American Journal of Ophthalmology*, **20**, 591–598.

Ryan, S. J. (1973). Cystoid maculopathy in phakic retinal detachment procedures. *American Journal of Ophthalmology*, **76**, 519–522.

Shea, M. (1968). Complications of cryotherapy in retinal detachment. *Canadian Journal of Ophthalmology*, **3**, 109–115.

Sudarsky, R. D., and Yanuzzi, L. A. (1970). Cryomarcation line and pigment migration after retinal cryosurgery. *Archives of Ophthalmology*, **83**, 395–401.

Tanenbaum, H. L., and Schepens, C. L. (1969). Macular pucker following retinal surgery: a biomicroscopic study. *Canadian Journal of Ophthalmology*, **4**, 20–23.

British Journal of Ophthalmology, 1978, **62**, 604–608

Von Hippel's disease in association with von Recklinghausen's neurofibromatosis

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SUMMARY Ten members of a large family who showed manifestations of either von Hippel-Lindau disease or von Recklinghausen's neurofibromatosis were examined. Three of 10 members were found to have retinal angiomas which had not been present on fundus examination 3 years previously. These angiomas were associated with ocular and systemic signs of neurofibromatosis. These cases show overlapping manifestations of different phakomatoses and provide support for the concept of a common aetiology for these diseases.

In 1923 Van der Hoeve introduced the term 'phakomatoses' to describe a heredofamilial group of diseases characterised by the presence of disseminated hamartomas (Van der Hoeve, 1923). The 6 diseases that constitute this group are tuberous sclerosis or Bourneville's disease, von Recklinghausen's neurofibromatosis, von Hippel-Lindau disease, meningocutaneous angiomatosis or Sturge-Weber syndrome, ataxia-telangiectasia or Louis-Bar syndrome, and arteriovenous communication of retina and brain or Wyburn-Mason syndrome (Yanoff and Fine, 1975). The term von Hippel's disease refers to retinal angiomatosis not occurring in association with a vascular tumour of the central nervous system. Similarities in inheritance patterns and affected germ layers have been noted among the phakomatoses. However, each has distinctive clinical features, and reports of overlapping manifestations of 2 phakomatoses in the same individual or family are uncommon (Fracassi and Parachu, 1935; Chapman *et al.*, 1959; Melmon and Rosen, 1964).

The present report adds 3 new cases of von Hippel's disease from a large family (Fig. 1) with known overlapping signs of von Hippel-Lindau disease and von Recklinghausen's neurofibromatosis.

Case reports

CASE 1

(Subject IV-17 in Fig. 1). A 17-year-old woman was admitted to a hospital at the age of 13 for evaluation of severe headaches and projectile vomiting. Physical examination at that time showed a normal blood pressure, numerous large café-au-lait spots, and axillary freckles. Cutaneous neurofibromas were not present. Ocular examination showed normal retinal vasculature in both fundi. Family history revealed that her mother had overlapping manifestations of Lindau's disease and von Recklinghausen's neurofibromatosis proved at necropsy. A pneumoencephalogram and ventriculogram showed hydrocephalus with aqueductal stenosis and a mass in the thalamic area on the left side. Owing to her skin lesions and the family history of neurofibromatosis the thalamic mass was thought to be a glioma, though a tissue diagnosis was not made. Radiation therapy was begun at this time. The patient's hospital course was complicated by meningitis, malfunctioning shunts, and paraplegia secondary to arachnoiditis.

At age 14 years ophthalmoscopic examination revealed a visual acuity of RE 10/30 and LE 12/30. The fundi were normal except for resolving papilloedema of the left optic disc. Two years after onset of symptoms the patient had marked limitation of intellectual and motor functions.

In March 1977 the patient was referred to the Massachusetts Eye and Ear Infirmary for evaluation of a 'greenish mass' in the left eye. Ocular examination showed a visual acuity of RE 20/50 and LE hand motions at 1 ft (30 cm). Forty-five prism dioptres of left exotropia and a Gunn pupillary reaction in the left eye were present. Slit-lamp examination revealed multiple iris naevi in both eyes. Fundus examination of the right eye showed retinal angiomas in 3 areas (Figs. 2, 3, 4). A non-rhegmatogenous retinal detachment sparing the

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macular area was present in both inferior quadrants and in the superonasal quadrant. Considerable vitreous membrane formation was present overlying the angiomas in the superonasal quadrant (Fig. 2).

Fundus examination of the left eye showed a long-standing total retinal detachment partially obscured by old vitreous haemorrhage. A red mass seen in the superonasal quadrant was thought to be a retinal angioma. The patient was admitted to hospital for surgical treatment of retinal detachment, and a preoperative neurological evaluation, including computerised axial tomography (CAT) scan, revealed a large left thalamic mass which was consistent with the diagnosis of thalamic glioma.

Cryotherapy of the retinal angiomas combined with scleral buckling was successfully performed on the right eye.

A shave skin biopsy of a café-au-lait spot from the left arm was obtained (Fig. 5) and sent for electron microscopic examination in order to establish a tissue diagnosis of von Recklinghausen's neurofibromatosis. This showed macromelanosomes in melanocytes of the epidermis (Fig. 6).

CASE 2

(Subject IV-18 in Fig. 1). A 14-year-old boy was examined 3 years before the present examination, at which time signs of neurofibromatosis were found, while both fundi appeared normal. CAT-scan examination 2 months previously was negative for intracranial lesions. The patient complained of occasional headaches but denied other neurological symptoms. He had no symptoms referable to his kidneys, adrenal glands, pancreas, or thyroid gland. His blood pressure was 130/80 mmHg. Examination of his skin showed more than 6 café-au-lait spots. One subcutaneous nodule was present on the right leg.

Ocular examination showed that the visual acuity was 20/25 in both eyes. Applanation tensions were 15 mmHg in the right eye and 19 mmHg in the left. On biomicroscopy numerous iris naevi were seen, and fundus examination showed retinal angiomas in both eyes (Figs. 7, 8).

CASE 3

(Subject IV-16 in Fig. 1). A 20-year-old woman was examined 3 years previously and was found to have signs of neurofibromatosis and normal ocular fundi. The patient complained of occasional headaches but denied other neurological symptoms. Her blood pressure was 158/84 mmHg. Examination of her skin showed 3 café-au-lait spots measuring greater than 1·5 cm each. Multiple small cutaneous neurofibromas were noted.

Ocular examination revealed a visual acuity of RE 20/20 and LE 20/25. Intraocular pressure by applanation tonometry was 21 mmHg in the right eye and 16 mmHg in the left eye. Slit-lamp examination showed numerous iris naevi. Ophthalmoscopy revealed a retinal angioma in the superonasal quadrant of the fundus of the right eye. The left fundus was within normal limits.

Discussion

The phakomatoses are syndromes of hereditary origin; all except the Louis-Bar syndrome are

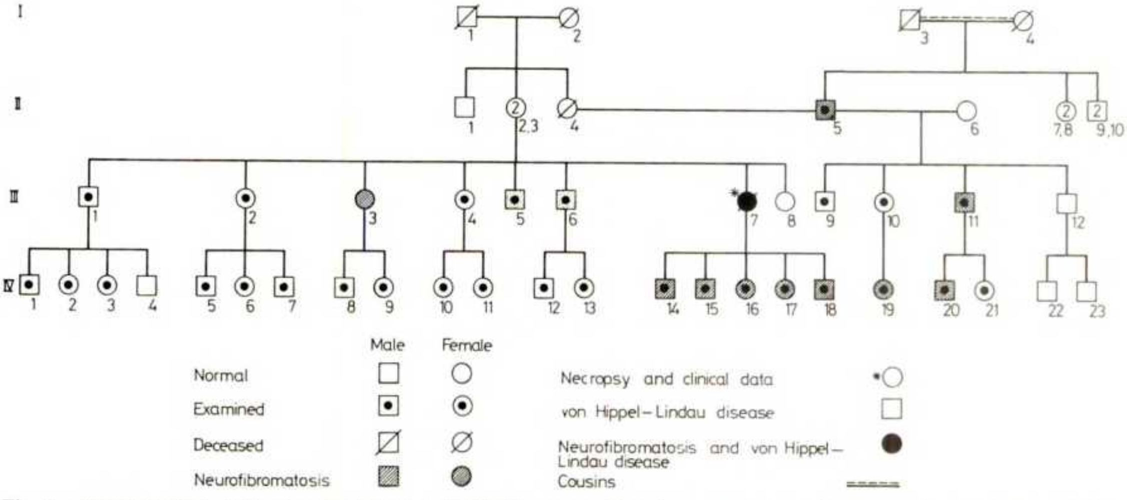
I
II
III
IV
Male
Female
Normal
Examined
Deceased
Neurofibromatosis
Necropsy and clinical data
von Hippel–Lindau disease
Neurofibromatosis and von Hippel–Lindau disease
Cousins

Fig. 1 *Pedigree of a family, certain members of which have von Recklinghausen's neurofibromatosis, von Hippel-Lindau disease, or a combined syndrome (reprinted from* Neurology, **25,** *840–4, with permission from Dr P. Tishler)*

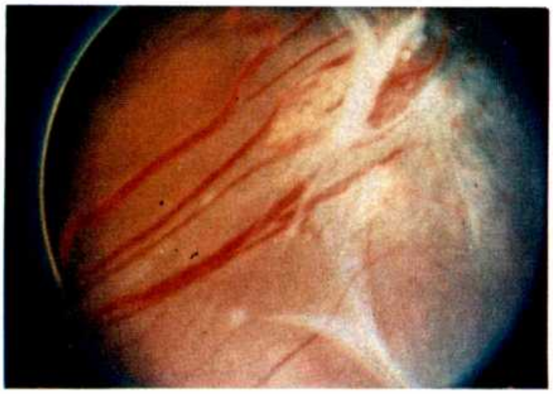

Fig. 2 *Retinal angiomas with dilated vessels and overlapping membranes in superonasal quadrant of right eye in Case 1*

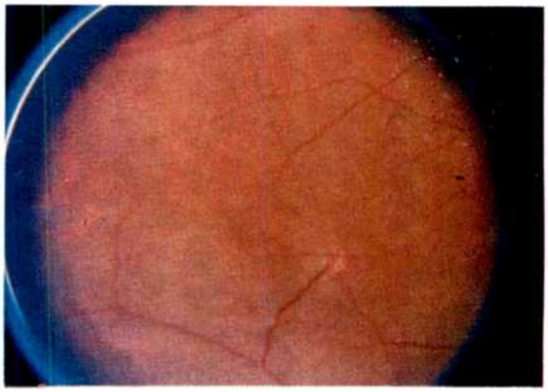

Fig. 3 *Retinal angioma in inferotemporal quadrant of right eye in Case 1*

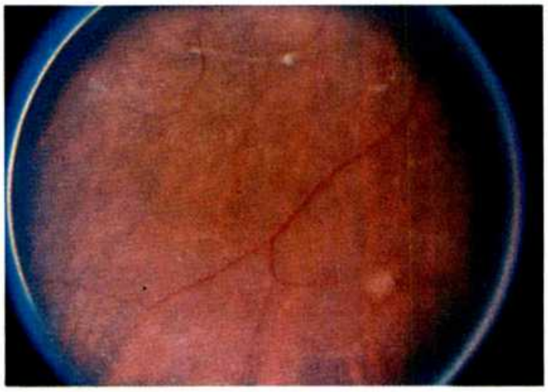

Fig. 4 *Retinal angioma in inferonasal quadrant of right eye in Case 1*

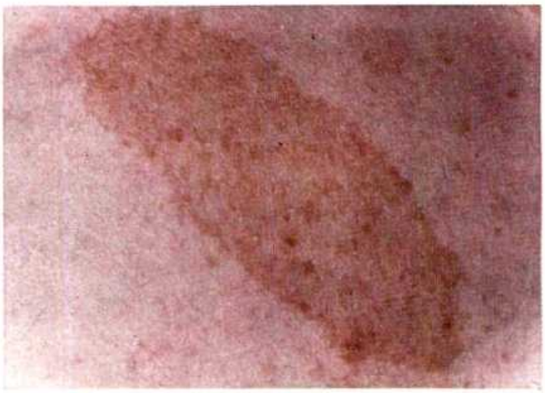

Fig. 5 *Typical café-au-lait spot in von Recklinghausen's neurofibromatosis from Case 1*

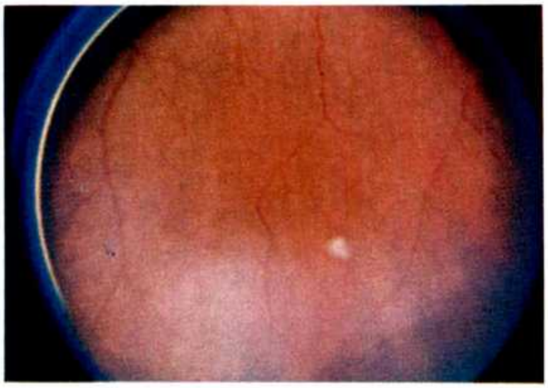

Fig. 7 *Retinal angioma in inferior portion of fundus of right eye in Case 2*

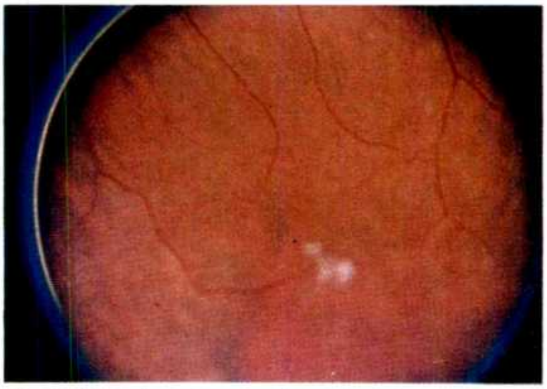

Fig. 8 *Retinal angioma in inferotemporal quadrant of fundus of left eye in Case 2*

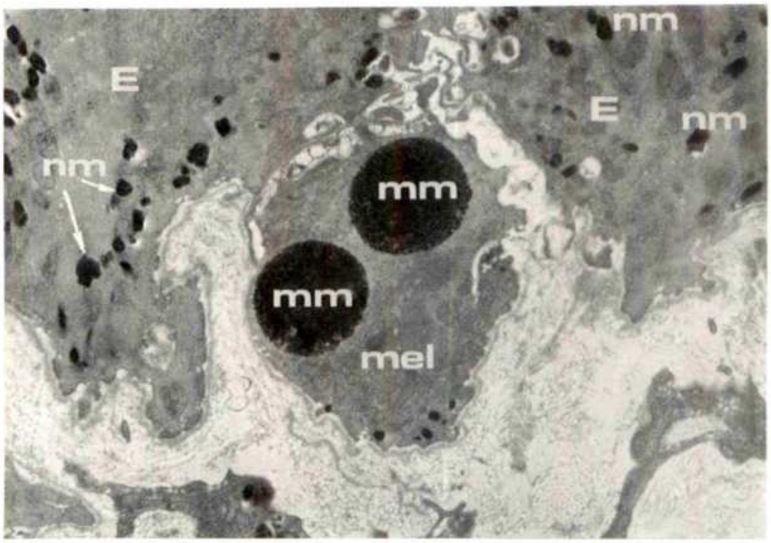

Fig. 6 *Electron micrograph of skin biopsy of café-au-lait spot in Case 1. Macromelanosomes (MM) in melanocyte (MEL) in epidermis are seen. Adjacent epidermal cells (E) containing melanosomes of normal size (NM) are present. Basement membrane separates epidermis from underlying dermis* (original magnification × 16 000)

transmitted in an autosomal dominant fashion. They are known to have individually characteristic clinical and pathological features which have been well described (Boder and Sedgwick, 1958; Alexander and Norman, 1960; Melmon and Rosen, 1964; Harley and Grover, 1970; Font and Ferry, 1972; Brown *et al.,* 1973). The clinical features of each phakomatosis reflect the abnormal development of predominantly 1 germ layer. Von Recklinghausen's neurofibromatosis and tuberous sclerosis may be considered to be mainly ectodermal abnormalities, while von Hippel-Lindau disease, Sturge-Weber syndrome, Louis-Bar syndrome, and Wyburn-Mason syndrome are characterised by abnormalities chiefly of mesoderm. It has been suggested that the phakomatoses are of embryodysplastic origin and that they show evidence of developmental errors in neuroectoderm and mesoderm, possibly at different stages of development (Waardenburg *et al.,* 1963). Cases in which clinical manifestations of two phakomatoses overlap in the same individual or family are of interest because they support the concept of a common aetiology for this entire group of disorders.

In a previous report of this family (Tishler, 1975) certain members were noted to have von Recklinghausen's neurofibromatosis while others had von Hippel-Lindau's disease. Only one individual had a combined syndrome (neurofibromatosis, café-au-lait spots, phaeochromocytomas, cerebellar haemangioblastoma, renal cell carcinoma, and pancreatic cysts). Re-examination of 10 members of this family showed retinal angiomas associated with von Recklinghausen's neurofibromatosis in 3 members. We found only 2 other patients with neurofibromatosis and retinal angiomas in the ophthalmic literature (Frenkel, 1967; Wolter, 1965). In the latter case the angiomas were solitary.

Von Recklinghausen's neurofibromatosis is known to involve the skin, nervous system, bones, endocrine glands, and eyes. The most striking clinical expression of the disease is the presence of café-au-lait spots. 80% of patients with neurofibromatosis can be diagnosed by the presence of more than six café-au-lait spots. From the remaining 20% those over 21 years of age will usually have multiple cutaneous tumours and few pigmented spots, while those under 21 years may have no dermal tumours and few pigmented spots (Adams and Reed, 1971). It is known that 10% of the normal population have 1 or more café-au-lait spots, and these pigmented skin lesions have also been reported in Albright's syndrome, a condition closely related to neurofibromatosis. Electron microscopic observations indicate that macromelanosomes are present in melanocytes in the café-au-lait spots of von Recklinghausen's neurofibromatosis (Jimbow *et al.,* 1973) but are absent in the café-au-lait spots of normal subjects (Johnson and Charneco, 1970) and in patients with Albright's syndrome (Benedict *et al.,* 1968).

Since in Case 1 the diagnosis of von Recklinghausen's neurofibromatosis was not confirmed by tissue diagnosis of the suspected thalamic glioma, a skin biopsy of a café-au-lait spot was performed. Electron microscopic examination of the biopsy specimen revealed macromelanosomes in melanocytes in the epidermis, thus confirming the diagnosis of neurofibromatosis.

The findings in von Hippel-Lindau disease include haemangioblastomas of the retina, cerebellum, medulla, and spinal cord, pancreatic cysts, renal cysts, hypernephromas, and rarely phaeochromocytomas. A clinical feature common to both diseases is the presence of phaeochromocytomas. These adrenal gland tumours are found in approximately 10% patients with neurofibromatosis, while they have been reported in only 9 cases in association with von Hippel-Lindau disease (Wise and Gibson, 1971).

Associations between the other phakomatoses have been previously described. Glial hamartomas of the retina and optic nerve head are known to occur in both von Recklinghausen's neurofibromatosis and tuberous sclerosis (Van der Hoeve, 1932). Neurofibromatosis has been reported in patients with tuberous sclerosis and in members of the same family (Kirby, 1951). Two coexisting conditions—tuberous sclerosis and a large vascular malformation over the left cerebral hemisphere—in 1 patient provide further evidence of association between phakomatoses (Chapman *et al.*, 1959). In addition adenoma sebaceum and Sturge-Weber syndrome have been reported to occur together in a father and his son (Frenkel, 1967). Tuberous sclerosis has been observed in the uncle of 2 siblings with Lindau's disease (Moller, 1952). Pancreatic cysts, kidney cysts, and hypernephromas are visceral manifestations common to both tuberous sclerosis and von Hippel-Lindau disease (Chapman *et al.*, 1959). The typical cavernous haemangioma or telangiectasis of the facial skin seen in Sturge-Weber syndrome has been described in a patient with Lindau's disease (Font and Ferry, 1972).

It is evident that such associations do exist and their total expression may not be evident during a preliminary examination. Although retinal angiomas are most frequently seen in early life, they may first appear in older individuals. Repeated ocular examinations of these patients are indicated in order to detect the vascular tumours at an early stage when complications have not yet developed and the management is relatively easy.

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References

Adams, R. D., and Reed, W. B. (1971). Neurocutaneous diseases. In *Dermatology in Internal Medicine*, pp. 1379–1434. Edited by T. B. Fitzpatrick, K. A. Arndt, and W. H. Clark. McGraw-Hill: New York.

Alexander, G. L., and Norman, R. M. (1960). The Sturge-Weber Syndrome. Wright: Bristol.

Benedict, P. H., Szabo, G., Fitzpatrick, T. B., and Sinesi, S. J. (1968). Melanotic macules in Albright's syndrome and in neurofibromatosis. *Journal of the American Medical Association*, **205**, 618–626.

Boder, E., and Sedgwick, R. P. (1958). Ataxia-telangiectasia. A familial syndrome of progressive cerebellar ataxia, oculo-cutaneous telangiectasia and frequent pulmonary infections. *Pediatrics*, **21**, 526–554.

Brown, D. G., Hilal, S. H., and Tenner, H. S. (1973). Wyburn-Mason syndrome. Report of two new cases without retinal involvement. *Archives of Neurology*, **28**, 67–69.

Chapman, R. C., Kempt, V. E., and Taliaferro, I. (1959). Pheochromocytoma associated with multiple neurofibromatosis and intracranial hemangioma. *American Journal of Medicine*, **26**, 883–890.

Font, R. L., and Ferry, A. P. (1972). The phakomatoses. *International Ophthalmology Clinics*, **12**, 1–50.

Fracassi, T., and Parachu, L. M. (1935). Angiomas del sisteima nervisos central: a proposito de siete casos observados. *Rev Argentina de Neurologia y Psiquiatria*, **1**, 58–81.

Frenkel, M. (1967). Retinal angiomatosis in a patient with neurofibromatosis. *American Journal of Ophthalmology*, **63**, 804–807.

Harley, R. D., and Grover, W. D. (1970). Tuberous sclerosis. Description and report of 12 cases. *Annals of Ophthalmology*, **1**, 477, 481.

Jimbow, K., Szabo, G., and Fitzpatrick, T. B. (1973). Ultrastructure of giant pigment granules (macromelanosomes) in the cutaneous pigmented macules of neurofibromatosis. *Journal of Investigative Dermatology*, **61**, 300–309.

Johnson, B. L., and Charneco, D. R. (1970). Café au lait spot in neurofibromatosis and in normal individuals. *Archives of Dermatology*, **102**, 442–446.

Kirby, T. J. (1951). Ocular phakomatoses. *American Journal of Medical Science*, **222**, 227–231.

Melmon, K. L., and Rosen, S. W. (1964). Lindau's disease: review of the literature and study of a large kindred. *American Journal of Medicine*, **36**, 595–617.

Moller, P. M. (1952). Another family with von Hippel-Lindau's disease. *Acta Ophthalmologica*, **30**, 155–165.

Tishler, P. V. (1975). A family with coexistent von Recklinghausen's neurofibromatosis and von Hippel-Lindau disease. Diseases possibly derived from a common gene. *Neurology*, **25**, 840–844.

Van der Hoeve, J. (1923). Eye diseases in tuberous sclerosis of the brain and in Recklinghausen's disease. *Transactions of the Ophthalmological Societies of the United Kingdom*, **43**, 534–541.

Van der Hoeve, J. (1932). Doyne Memorial Lecture: eye symptoms in phakomatoses. *Transactions of the Ophthalmological Societies of the United Kingdom*, **52**, 380–401.

Waardenburg, P. J., Franceschetti, A., and Klein, D. (1963). *Genetics and Ophthalmology*, p. 1400. Royal van Gorcum: Assen.

Wise, K. S., and Gibson, J. A. (1971). Von Hippel-Lindau's disease and pheochromocytoma. *British Medical Journal*, **1**, 44.

Wolter, J. R. (1965). Nerve fibrils in ovoid bodies with neurofibromatosis of the choroid. *Archives of Ophthalmology*, **73**, 696–699.

Yanoff, M. Y., and Fine, B. S. (1975). *Ocular Pathology—A Text and Atlas*, 1st edn. pp. 30–38. Harper & Row: Maryland.

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Placoid pigment epitheliopathy and Harada's disease

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SUMMARY Twenty-six patients are described who suffered from acute bilateral multifocal pigment epithelial disease. In 7 the pattern of disease was indistinguishable from acute posterior multifocal placoid pigment epitheliopathy, while in 8 it was indistinguishable from Harada's disease. In a further 9 cases the pigment epithelial disease was associated with serous detachment of the retina simulating Harada's disease but without systemic symptoms; spontaneous resolution occurred within a few days, and there was no recurrence. One additional case had short-lived disease with detachment initially, but this was followed by severe recurrence, and the last patient had serous detachment in 1 eye but not the other. When seen as a whole these patients appeared to represent a continuous spectrum of disease making it difficult to define boundaries between one condition and another. The difficulties in distinguishing diseases according to morphology alone are emphasised.

During the last 5 years 26 patients have been seen at Moorfields Eye Hospital with acute multifocal disease affecting the retinal pigment epithelium bilaterally; all but 1 have been observed for at least 1 year. In some the characteristics of the disease were typical of Harada's disease (Harada, 1925; Shimizu, 1973) and in others were similar to those of acute posterior multifocal placoid pigment epitheliopathy (APMPPE) (Gass, 1968; van Buskirk *et al.*, 1971; Kirkham *et al.*, 1972). In the remaining patients the retinal morphology and course of the illness were similar in certain respects to Harada's disease and in others to APMPPE (Bird and Hamilton,1972). The attributes of these diseases will be described.

Results

Seven patients had acute bilateral pigment epithelial disease without serous retinal detachment which conformed to the description by Gass (1968) of APMPPE (Table 1). These patients presented with the acute onset of bilateral visual loss associated with multifocal, grey-white lesions in the posterior pole at the level of the retinal pigment epithelium. During the initial transit of fluorescein angiography these placoid lesions were darker than the normal background choroidal fluorescence (Fig. 1*a*), but in some large choroidal vessels were visible in the areas of hypofluorescence (Figs. 2*a*, *b*). Later in the study these lesions became hyperfluorescent (Figs. 1*b*, 2*c*). The swelling resolved spontaneously within 2 to 4 weeks without treatment in 6 patients, and in the same length of time in the 1 patient who received systemic corticosteroids. Visual recovery tended to take longer (2 to 12 weeks) and even then was incomplete in some cases. Only scattered areas of depigmentation or pigment clumping remained at the sites of the previous placoid lesions. The only systemic associations were genetically determined angioedema in 1 patient and myotonic dystrophy in another.

Seven patients (Cases 8 to 14) had severe acute bilateral disease affecting the retinal pigment epithelium, extensive serous retinal detachment, and other abnormalities associated with Harada's disease, including uveitis, papillitis, tinnitus, headache, and alopecia (Table 1). The appearance during the initial transit of fluorescein angiography was identical to that in APMPPE (Figs. 3*a*, *b*), but during the subsequent 5 minutes there was progressive accumulation of dye in the subretinal space (Fig. 3*c*). The pattern of choroidal filling when it could be seen was suggestive of slow perfusion of the choriocapillaris. Within 1 week there were no signs of spontaneous resolution of the detachment. All 7 patients were treated with systemic corticosteroids, and flattening of the retina occurred within 2 to 6 weeks. Five of these patients were Caucasians and

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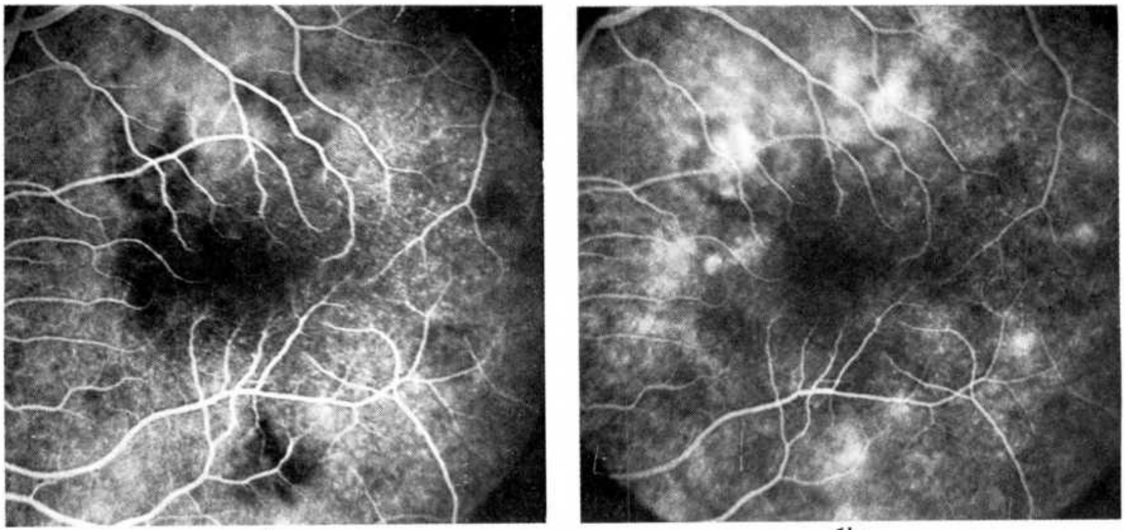
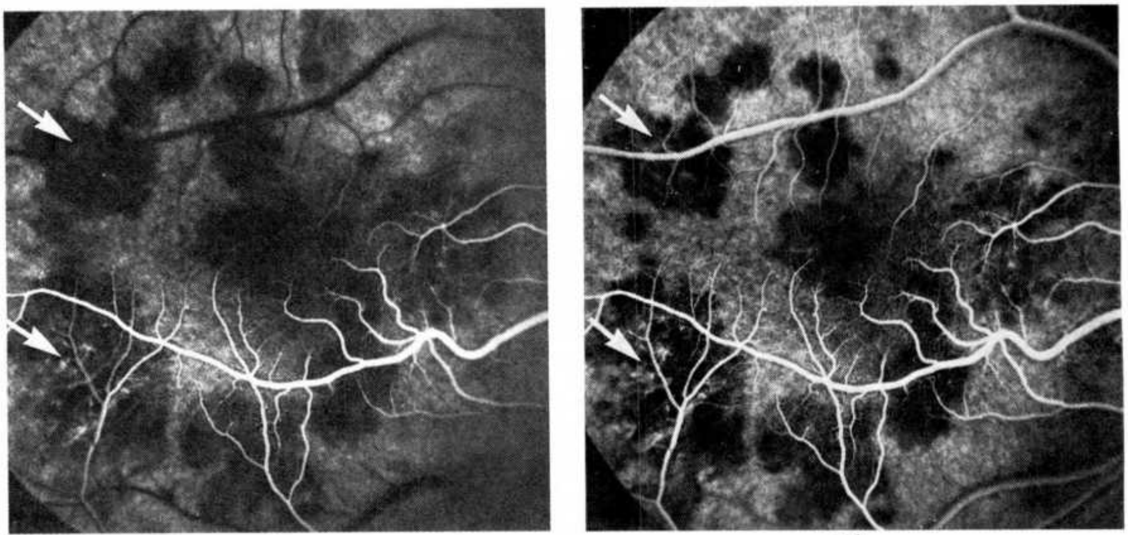


1a 1b

Fig. 1 *Case 5. Fluorescein angiography 6 days after initial visual loss showing dark patches during the initial transit of dye* (Fig. 1*a*) *with progressive accumulation of fluorescein in these areas during the subsequent 5 minutes* (Fig. 1*b*)



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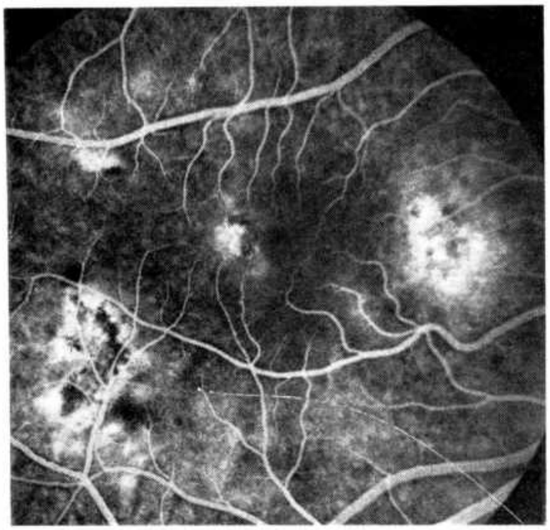
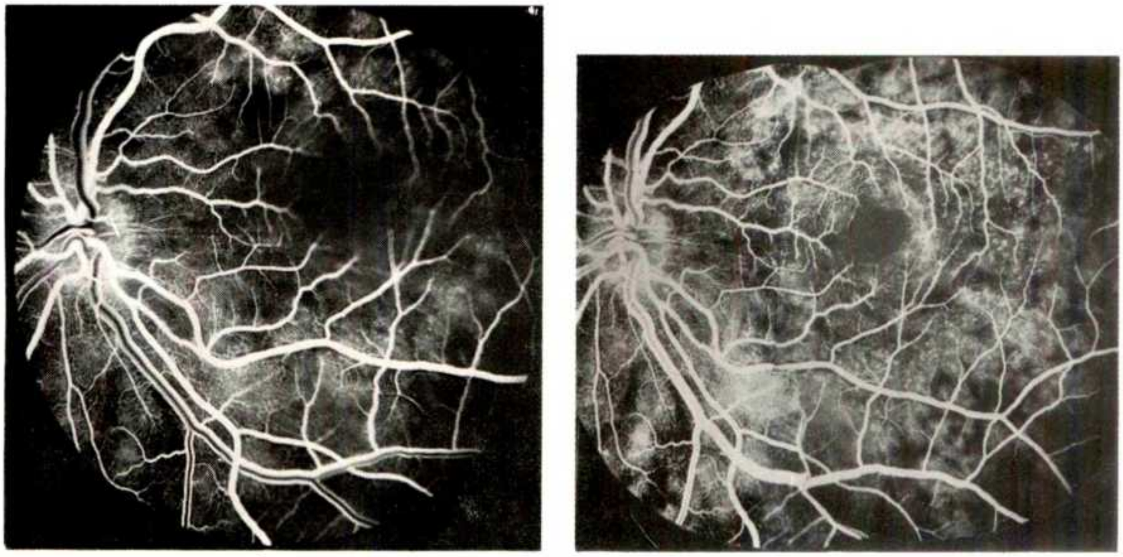


2c

Fig. 2 *Case 3. Twelve days after initial visual loss. Fluorescein angiography shows dark patches in the choroid during the initial transit, but all choroidal vessels can be seen within these areas* (Fig. 2*a, b*). *During the subsequent 5 minutes these areas became hyperfluorescent* (Fig. 2*c*)

2 Mongolians. Of the 6 patients available for follow-up all suffered later recurrences which also required corticosteroid therapy. One additional Mongolian patient seen with this syndrome did not receive systemic corticosteroids because of medical contraindications, and the ocular changes took 6 weeks to resolve; this patient has not yet suffered a recurrence.

Nine further patients presented with the acute onset of bilateral visual loss associated with multifocal placoid, grey-white lesions in the posterior pole at the level of the retinal pigment epithelium


3a 3b

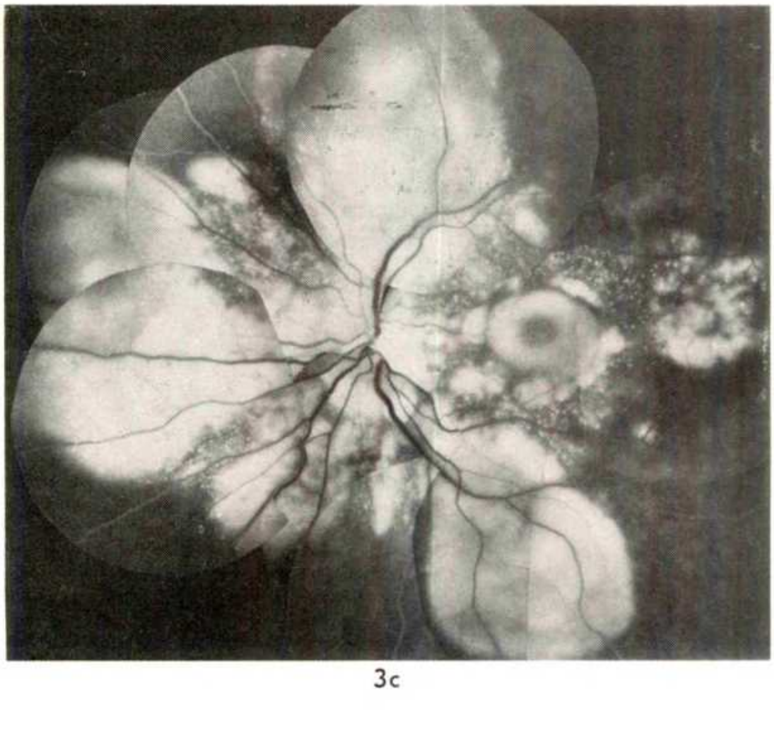
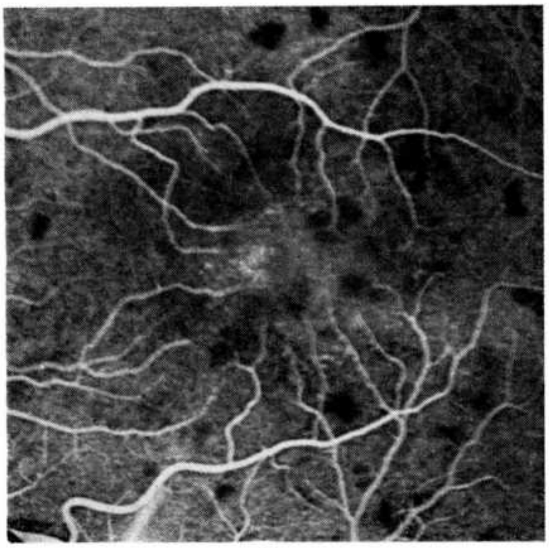
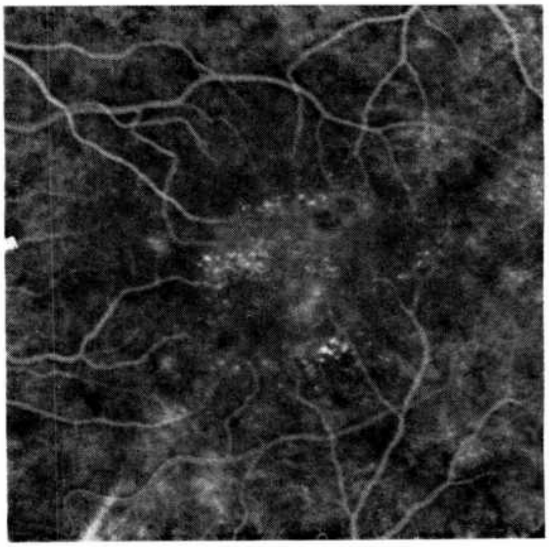

3c

Fig. 3 *Case 12. Three days following initial visual loss. Fluorescein angiography shows dark patches in the choriocapillaris during the initial transit of dye and subsequent progressive accumulation of dye within the pigment epithelium and subretinal space during the subsequent 5 minutes*

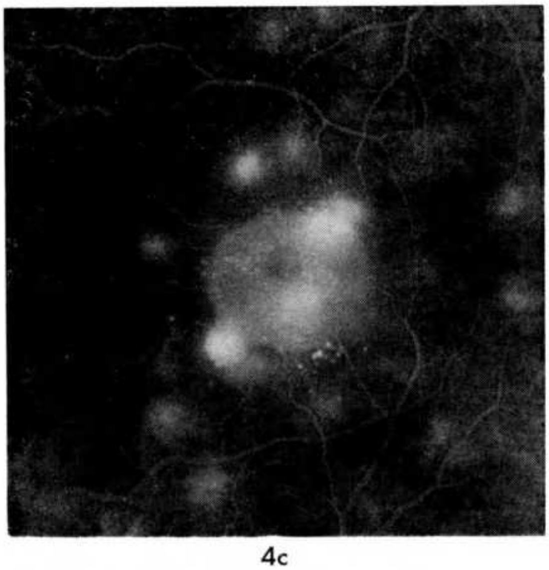
and overlying serous retinal detachment. The fluorescein angiograms were indistinguishable from those seen in Harada's disease, though the serous retinal detachment was usually less extensive (Figs. 4*a*, *b*, *c*; 5*a*, *b*; 6*a*, *b*; 7). The disease differed from classical Harada's disease in that partial or complete spontaneous retinal reattachment occurred within 1 week (Figs. 5*c*; 6*c*–*g*; 7); despite this 3 patients subsequently received systemic corticosteroids. The serous retinal detachment resolved within 2 weeks in all patients, leaving pigment epithelial lesions beneath flat retina. At this stage the fundus appearance was indistinguishable from APMPPE during the recovery phase. In 1 case slow perfusion of the choriocapillaris was demonstrated during the recovery phase on fluorescein angiography (Figs. 6*c*–*g*) (Bird and Hamilton, 1972). Visual recovery was complete within another 4 weeks. Signs of inflammation were identified in most, but other features, namely, tinnitus, dysacousis, alopecia, poliosis, and vitiligo, were absent (Table 1). In none of these cases has the disease recurred.



4a



4b



4c

Fig. 4 *Case 19. Three days following initial visual loss. Fluorescein angiography showing dark areas in the choroid during the initial transit of dye* (Fig. 4*a*) *with subsequent accumulation of dye in the pigment epithelium and subretinal space* (Fig. 4*a*, *b*, *c*)

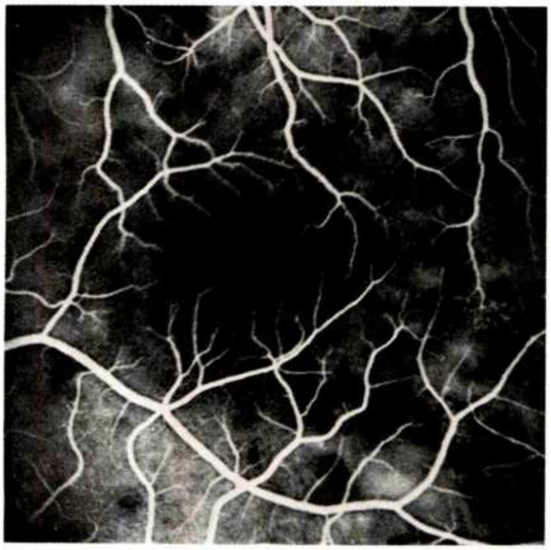
One further case (25) was seen with acute pigment epithelial lesions and limited serous retinal detachment, which resolved spontaneously within 2 weeks. However, this patient suffered several recurrences of much more severe disease necessitating the use of systemic corticosteroids.

The last case (26) had typical placoid pigment epitheliitis in her left eye when first seen, but the posterior retina was detached in the right. Spontaneous retinal flattening occurred within 1 week of presentation.

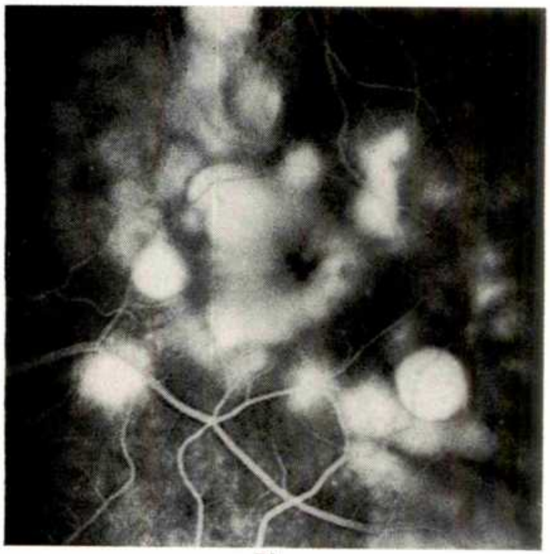
Discussion

The acute bilateral disease of the retinal pigment epithelium without serous retinal detachment followed by spontaneous resolution within 2 to 4 weeks, and the lack of recurrence in the first 7 patients, clearly conform to Gass's description of acute posterior multifocal placoid pigment epitheliopathy (1968).

Patients 8 to 15 (Table 1), who had widespread serous retinal detachment accompanying the acute



5a



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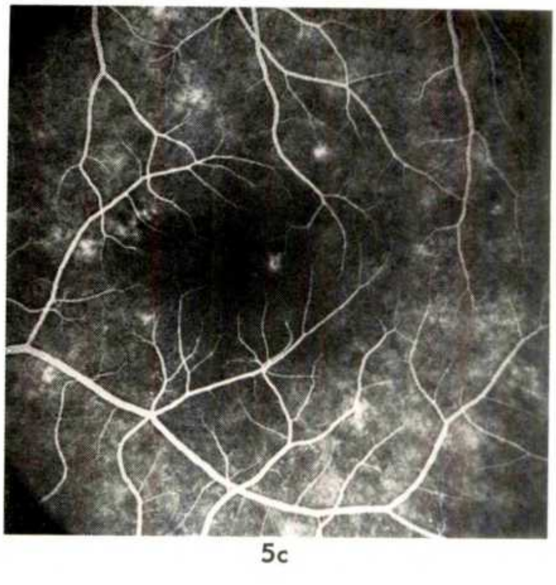
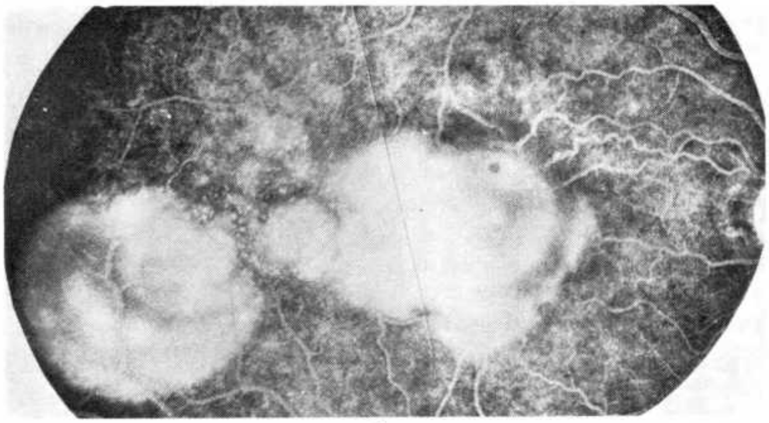
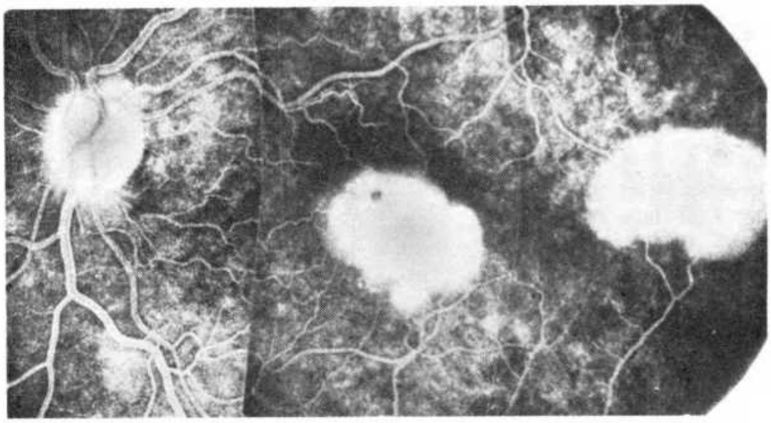


5c

Fig. 5 *Case 21. Fluorescein angiography showing dark patches in the choriocapillaris during the initial transit of dye* (Fig. 5*a*) *and subsequent accumulation of dye in the pigment epithelium and subretinal spaces* (Fig. 5*b*). *Ten days later the retina had settled spontaneously leaving pigment epithelial changes only* (Fig. 5*c*)



6a



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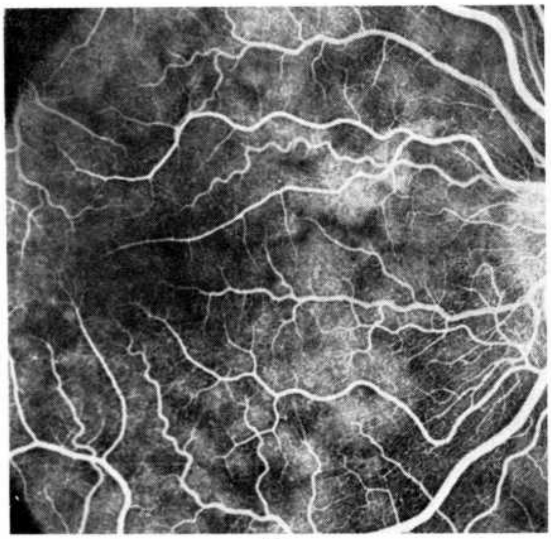

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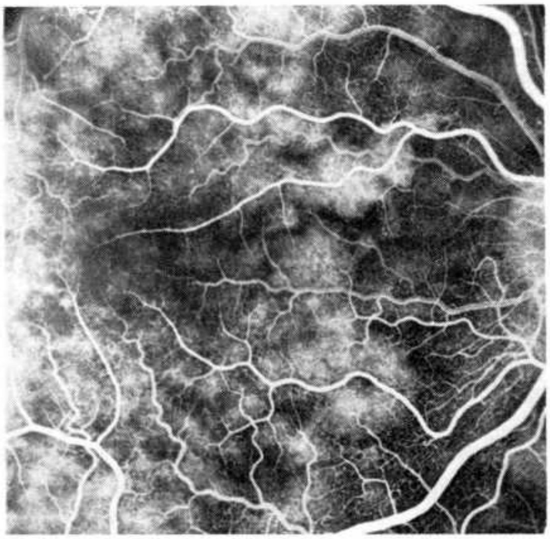
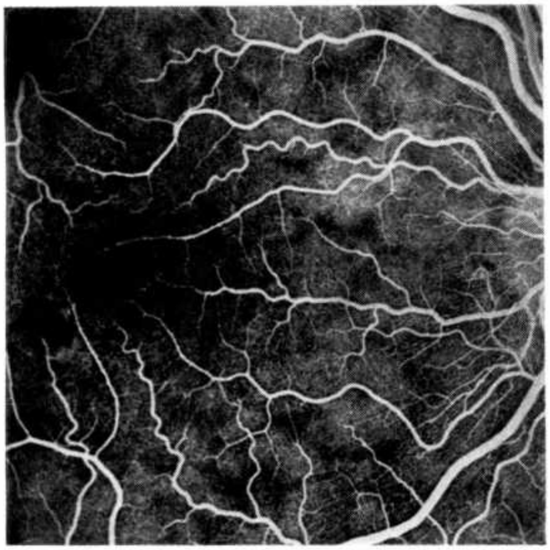


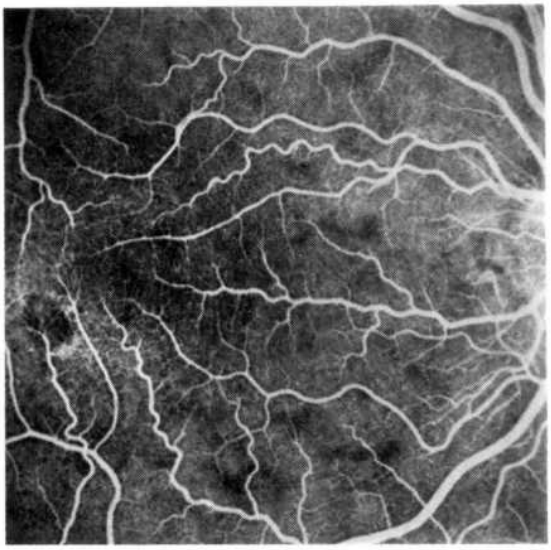
6d

multifocal pigment epithelial lesions and associated with uveitis, papillitis, tinnitus, headache, and alopecia, had disease similar to that described by Harada (1925), although 5 of our 8 cases occurred in Caucasians. No signs of recovery were identified within the first week, and all patients but one were given systemic corticosteroids. The disease in these patients was characterised by multiple recurrences, each requiring treatment.

As described, Harada's disease and APMPPE appear to be clearly different one from another in respect of their morphology and the subsequent behaviour of the disease. Nevertheless both present with acute multifocal pigment epithelial disease, and the changes identified during the initial fluorescein transit are indistinguishable; optic disc swelling is characteristic of Harada's disease and occurs in some patients with APMPPE. After recovery both show retinal pigment epithelial change; in APMPPE the changes are multifocal, with profound atrophy of the retina and choroid in some, whereas in Harada's disease they are diffuse.

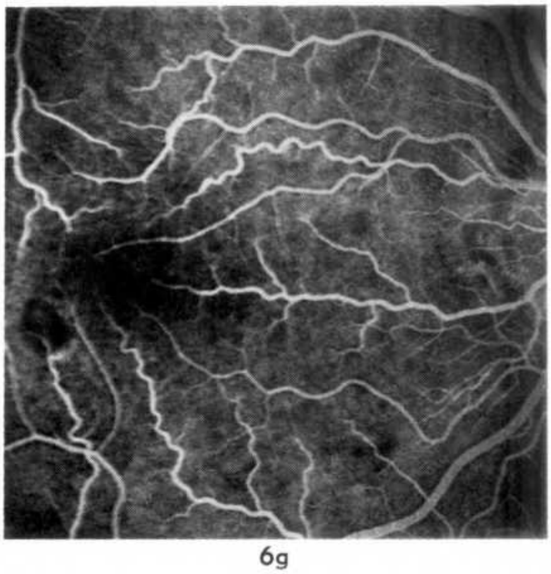


6e



6f

Fig. 6 *Case 20. Four days after initial visual loss. Fluorescein angiography outlining limited retinal detachment at the posterior pole of each eye 5 minutes after initial dye entry* (Fig. 6*a*, *b*). *Within 18 days vision had recovered and the retina was flat. Fluorescein angiography showed slow filling of the choriocapillaris* (Fig. 6*c*–*g*)



6g

The pathogenesis of neither disease is known, and no specific test is available to distinguish one from the other. No histopathological material is available on APMPPE, but the association of this disease with erythema nodosum (van Buskirk *et al.*, 1971) suggests that the disease may be caused by a vasculitis affecting the choroidal arteries or arterioles and that the focal pigment epithelial lesions may represent infarcts, a view supported by Deutman *et al.* (1972). The appearance of the large choroidal vessels in the areas of hypofluorescence during the initial transit of dye on fluorescein angiography in some patients (Figs. 2*a*, *b*) indicates that obstruction of choroidal fluorescence by swollen pigment epithelium cannot entirely explain hypofluorescence and that focal non-perfusion of the choriocapillaris occurs during the acute stage of the disease. Deutman and Lion (1976) have made similar observations. While the aetiology is unknown, viral disease has been implicated (Azur *et al.*, 1975), and many observers have reported an antecedent viral illness, either upper respiratory or gastrointestinal (Ryan

Table 1

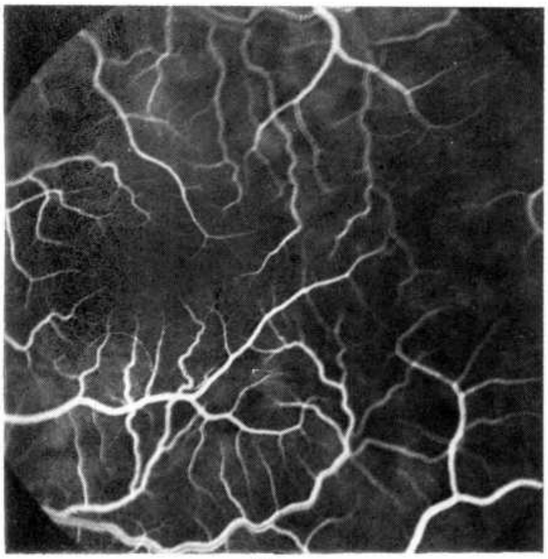
APMPPE	*Age*	*Interval to visual improvement to 6/9*	*Treatment with systemic corticosteroids*	*Recurrence*	*Associated findings*
1	52	2 weeks	+	–	Uveitis
2	38	2 weeks	–	–	Myotonic dystrophy
3	17	2 weeks	–	–	Genetically determined angioedema
4	15	3 weeks	–	–	–
5	32	3 weeks	–	–	—
6	31	2 weeks	–	–	—
7	24	2 weeks	–	–	—
Harada's					
8	31	6 weeks	+	+	Uveitis, headache, poliosis, viteligo, alopecia
9	38	3 weeks	+	+	Uveitis, headache, dysacousis, meningitis
10	45	3 weeks	+	+	Uveitis, headache, dysacousis, alopecia
11	36	2 weeks	+	+	Uveitis, papillitis, dysacousis
12	38	3 weeks	+	+	Uveitis, alopecia, viteligo
13	31	2 weeks	+	+	Uveitis, tinnitus, headache
14	48	6 weeks	Med. contraindications	–	Uveitis, headache, alopecia
15	26	6 weeks	+	+	Uveitis, headache, dysacousis
Intermediate					
16	24	1 week	+	–	Uveitis, papillitis, headache
17	34	6 days	–	–	—
18	34	2 weeks	+	–	Uveitis, papillitis, episcleritis, headache
19	21	1 week	–	–	—
20	26	2 weeks	+	–	Uveitis, headache
21	23	1 week	–	–	—
22	29	1 week	–	–	Uveitis
23	39	2 weeks	–	–	Uveitis
24	21	1½ weeks	–	–	Uveitis
25	28	5 days	–	+	Uveitis, headache, viteligo
26	20	2 weeks	–	–	Uveitis

and Maumenee, 1972; Annesley *et al.*, 1973; Fitzpatrick and Robertson, 1973; Savino *et al.*, 1974; Holt *et al.*, 1976).

In Harada's disease there is extensive lymphocytic and plasma cell infiltration of the choroid and proliferation of epithelioid cells with the formation of granulomatous nodular lesions (Woods, 1961; Hogan and Zimmerman, 1962). Involvement of the leptomeninges of the optic nerve by such an infiltration has also been reported (Perry and Font, 1977). This severe inflammatory reaction in the uveal tract results in profound disturbance of the retinal pigment epithelium and the accumulation of large amounts of subretinal fluid. The mechanisms by which the choroidal inflammation affects the retinal pigment epithelium have not been identified. The aetiology is unknown, although viral disease (Sugiura *et al.*, 1953; Morris and Schlaegal, 1964) and a disturbed immunological state (Hammer, 1971; Hammer, 1974) have been suggested.

Patients 16 to 24 when first seen had disease morphologically indistinguishable from Harada's disease, but unlike our concept of Harada's disease the course of the disease was brief, the patients did not have associated generalised disturbance, and the disease did not recur. Furthermore, the only feature which distinguished these patients from those with APMPPE was the presence of serous retinal detachment. The serous detachment resolved spontaneously and rapidly, leaving a fundus appearance similar to APMPPE in some. Fluorescein angiography during recovery in 1 patient (Figs. 6*c*–*g*) was identical to that seen in some cases of APMPPE (van Buskirk *et al.*, 1971) and indicates strongly that decreased perfusion of the choroid existed, at least in this patient.

When viewed as a whole, these patients appear to present a continuum of disease rather than separate disease entities. This impression is strengthened by patient 25, who when first seen had a brief episode of disease which resolved spontaneously, followed 3 months later by a severe recurrence



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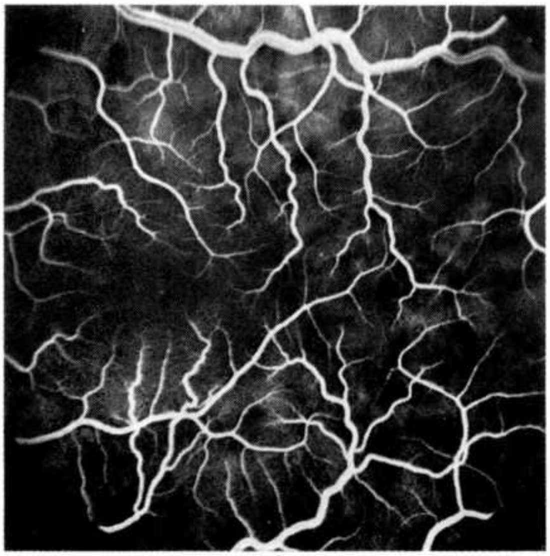

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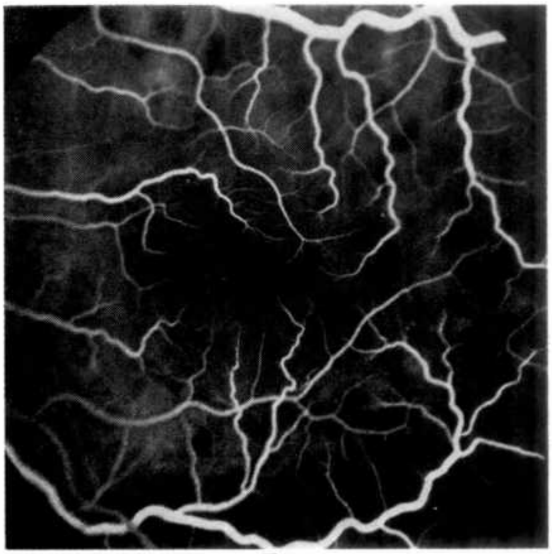

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typical of Harada's disease which required treatment with systemic corticosteroids. Patient 26 further confuses the differentiation of one disease from another since she had serous detachment in 1 eye but not the other.

Nevertheless, some of the patients described in this paper differ from others in many important respects, suggesting that more than one disease process might be involved. It is conceivable that those patients with serous retinal detachment (8 to 26) all fall within the spectrum of Harada's disease and that many had a more benign course than we

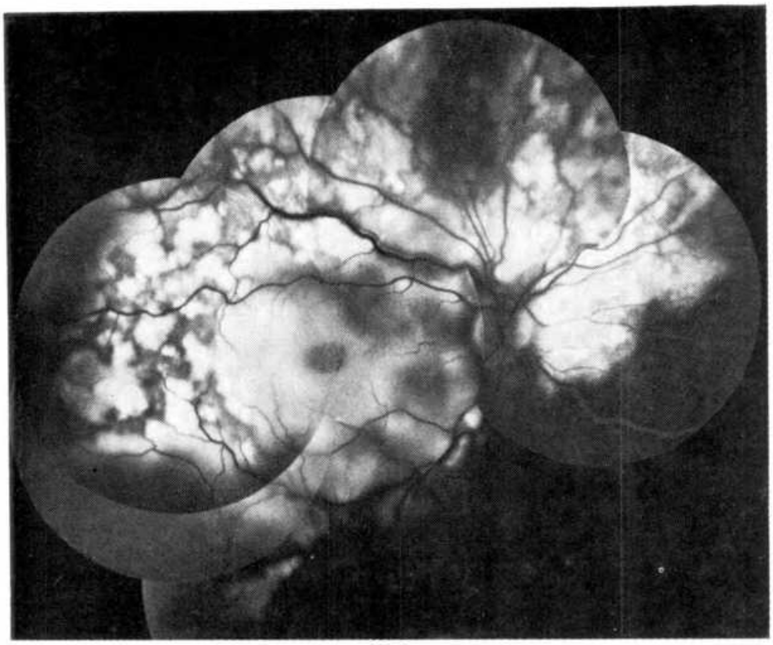

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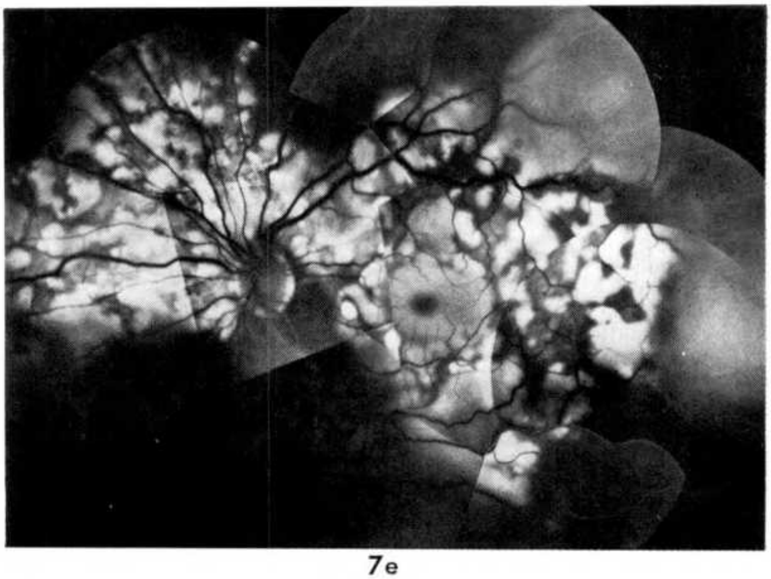
Fig. 7 *Case 23. Four days after onset of visual loss. Fluorescein angiography demonstrating apparent slow filling of the choriocapillaris* (Fig. 7*a–c*) *and progressive accumulation of dye in the subretinal space* (Fig. 7*d, e*). *Five days later the retinal detachment largely resolved with visual recovery and within a further week the retina was quite flat* (Fig. 7*g–i*)



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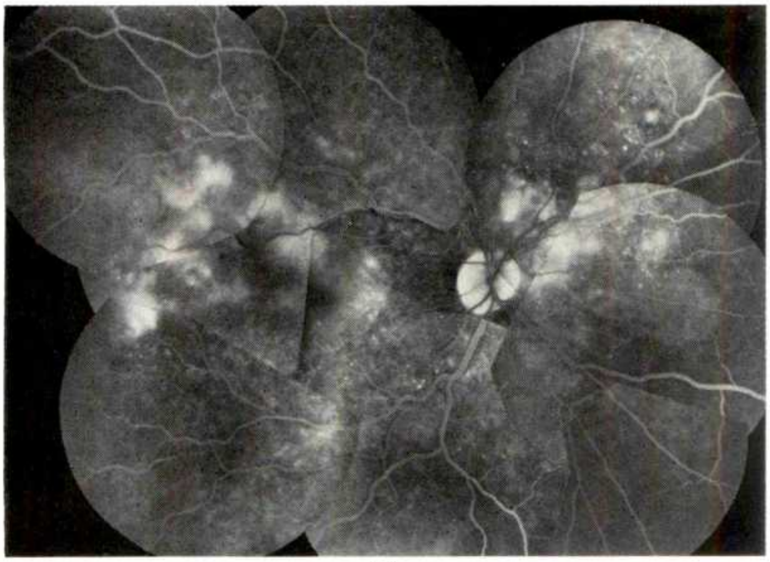
would have expected. The relatively benign nature of the disease in some patients has been emphasised by previous authors (Salus, 1932; Woods, 1961; Ohno *et al.*, 1977). If the disease behaves differently in different races (Ohno *et al.*, 1977), the presence of the 3 non-Caucasians in the severely affected group is significant. Alternatively, the intermediate group may be part of the spectrum of APMPPE in which serous retinal detachment occurs, as was implied by Bird and Hamilton (1972) and Holt *et al.* (1976). It is also possible that 3 or more separate disease entities could have caused the disorders in these patients. The apparent similarities in dissimilar diseases would be understandable if the clinical manifestations were due to a mechanism common to all, possibly poor choroidal perfusion and focal retinal pigment epithelial infarction. Finally, all may fall within the spectrum of a single



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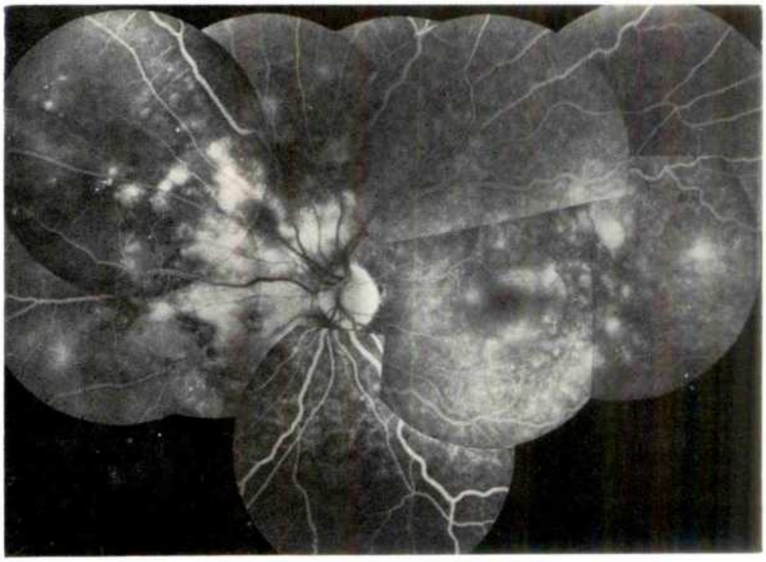

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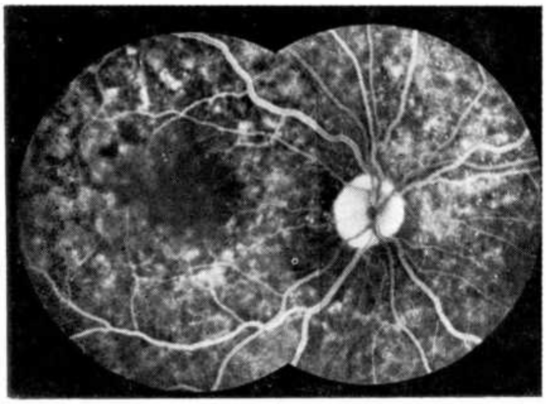
disease entity, a possibility alluded to by Ohno and co-workers (1977).

There is no doubt that the identification of a specific disease is helpful in determining a patient's visual prognosis, and that the definition of single disease entities within a group of disorders is important for research. However, it is apparent that a single disease can produce a variety of manifestations, as shown by onchocerciasis (Bird *et al.*, 1976), and equally that different diseases may present similar appearances. Harada's disease may be mimicked by sympathetic ophthalmia (Shimizu, 1973) and by scleritis (Cleary *et al.*, 1975), and the changes in pigment epitheliitis are similar to a single lesion in APMPPE (Krill and Deutman, 1972). Until the specific cause of a disease is determined and becomes identifiable in each patient, the classification of disease can be based only on its morphology, but the limitations of this basis for classification cannot be ignored.



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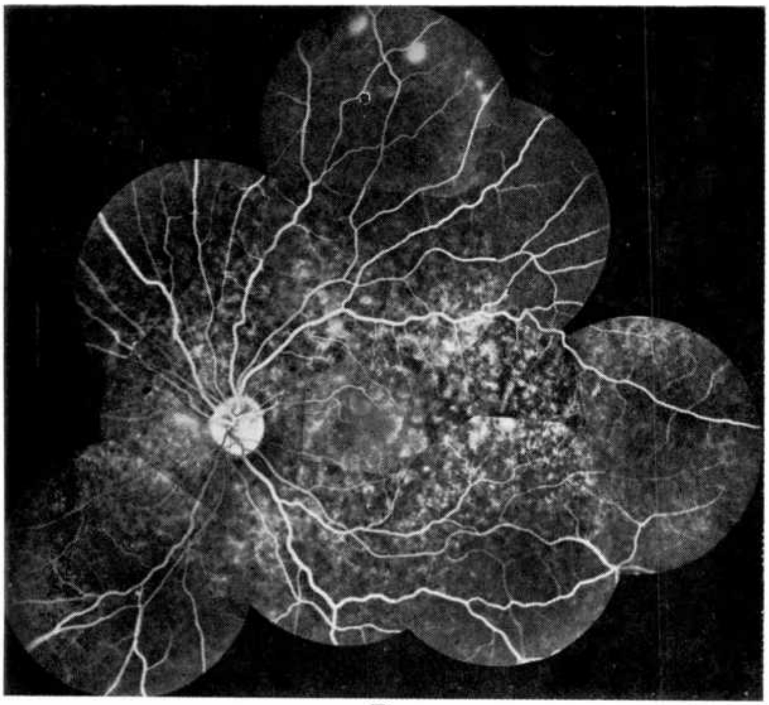

7i

We thank Mr K. S. Sehmi for his photographic expertise and Miss Jayne Fisher for secretarial assistance.

References

Annesley, W. H., Tomer, T. L., and Shields, J. A. (1973). Multifocal placoid pigment epithelialopathy. *American Journal of Ophthalmology*, **76**, 511–518.

Azur, P., Gohd, R. S., Waltman, D., and Gitter, K. A. (1975). Acute posterior multifocal placoid pigment epitheliopathy associated with an adenovirus type 5 infection. *American Journal of Ophthalmology*, **80**, 1003–1005.

Bird, A. C., and Hamilton, A. M. (1972). Placoid pigment epitheliopathy presenting with bilateral serous retinal detachment. *British Journal of Ophthalmology*, **56**, 881–886.

Bird, A. C., Anderson, J., and Fuglsang, H. (1976). Morphology of posterior segment lesions of the eye in patients with onchocerciasis. *British Journal of Ophthalmology*, **60**, 2–20.

Cleary, P. E., Watson, P. G., McGill, J. I., and Hamilton, A. M. (1975). Visual loss due to posterior segment disease in scleritis. *Transactions of the Ophthalmological Societies of the United Kingdom*, **95**, 297–300.

Deutman, A. F., Oosterhuis, J. A., Boen-Tan, T. N., and Aan de Kerk, A. I. (1972). Acute posterior multifocal placoid pigment epitheliopathy. *British Journal of Ophthalmology*, **56**, 863–874.

Deutman, A. F., and Lion, F. (1976). Acute multifocal placoid pigment epitheliopathy. *American Journal of Ophthalmology*, **84**, 652–658.

Fitzpatrick, P. J., and Robertson, D. M. (1973). Acute posterior multifocal placoid pigment epitheliopathy. *Archives of Ophthalmology*, **89**, 373–376.

Gass, J. D. M. (1968). Acute posterior multifocal placoid pigment epitheliopathy. *Archives of Ophthalmology*, **80**, 177–185.

Hammer, H. (1971). Lymphocyte transformation test in sympathetic ophthalmitis and the Vogt-Koyanagi-Harada syndrome. *British Journal of Ophthalmology*, **55**, 850–852.

Hammer, H. (1974). Cellular hypersensitivity to uveal pigment confirmed by leucocyte migration tests in sympathetic ophthalmitis and the Vogt-Koyanagi-Harada syndrome. *British Journal of Ophthalmology*, **58**, 773–776.

Harada, E. (1925). Additional report upon acute bilateral choroiditis followed by retinal detachment. *Japanese Journal of Clinical Ophthalmology*, **20**, 157.

Hogan, M. J., and Zimmerman, L. E. (1962). *Ophthalmic Pathology*, 2nd edn., pp. 398–400. Saunders: Philadelphia.

Holt, W. S., Regan, C. D. J., and Trempe, C. (1976). Acute posterior multifocal placoid pigment epitheliopathy. *American Journal of Ophthalmology*, **81**, 403–412.

Kirkham, T. H., ffytche, T. J., and Sanders, M. D. (1972). Placoid pigment epitheliopathy with retinal vasculitis and papillitis. *British Journal of Ophthalmology*, **56**, 875–880.

Krill, A. E., and Deutman, A. F. (1972). Acute retinal pigment epithelitis. *American Journal of Ophthalmology*, **74**, 193–205.

Morris, W. R., and Schlaegel, T. F. (1964). Virus-like inclusion bodies in subretinal fluid in uveo-encephalitis. *American Journal of Ophthalmology*, **58**, 940–945.

Ohno, S., Char, D. H., Kimura, S. J., and O'Connor, G. R. (1977). Vogt-Koyanagi-Harada syndrome. *American Journal of Ophthalmology*, **83**, 735–740.

Perry, H. D., and Font, R. L. (1977). Clinical and histopathologic observations in severe Vogt-Koyanagi-Harada syndrome. *American Journal of Ophthalmology*, **83**, 242–254.

Ryan, S. J., and Maumenee, A. E. (1972). Acute posterior multifocal placoid pigment epitheliopathy. *American Journal of Ophthalmology*, **74**, 1066–1074.

Salus, R. (1932). Harada, seheKrankheit. *Klinische Monatsblätter für Augenheilkunde*, **89**, 84–87.

Savino, P., Weinbert, R., Yassin, J., and Pilkerton, A. R. (1974). Diverse manifestations of acute posterior multifocal placoid pigment epitheliopathy. *American Journal of Ophthalmology*, **77**, 659–662.

Shimizu, K. (1973). Harada's, Behçet's, Vogt-Koyanagi syndromes—are they clinical entities? *Transactions of the American Academy of Ophthalmology and Otolaryngology*, **77**, 281–290.

Sugiura, S., Fukuda, M., and Eda, K. (1953). The viral nature of the Harada-Vogt-Koyanagi syndrome. *Acta Societatis Ophthalmologicae Japonicae*, **57**, 117.

Van Buskirk, E. M. A., Lessell, S., and Friedman, E. (1971). Pigmentary epitheliopathy and erythema nodosum. *Archives of Ophthalmology*, **85**, 369–372.

Woods, A. C. (1961). *Endogenous Inflammations of the Uveal Tract*, pp. 267–273. Williams and Wilkins: Baltimore.

British Journal of Ophthalmology, 1978, **62**, 622–626

Fundus changes in incontinentia pigmenti (Bloch-Sulzberger syndrome): a case report

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SUMMARY A case of incontinentia pigmenti is reported with fundus changes in 1 eye. She had microaneurysms temporal to the macula, with an abnormal branch of inferior temporal vein. There was extensive retinitis proliferans in the upper temporal equatorial region, which showed leakage on fluorescein angiography.

The ocular and systemic changes in incontinentia pigmenti are reviewed here and a case is reported with fundus changes which have not been described previously.

Incontinentia pigmenti (IP) is characterised by ectodermal defects, with occasional associated mesodermal abnormalities. The typical skin lesions are blue-grey to chocolate-brown arranged along the naevus lines of Blaschko. These occur on the torso and the extremities. The disease can be differentiated into 2 clinical types: Bloch-Sulzberger and Naegeli. The Bloch-Sulzberger syndrome occurs predominantly in females and is usually present at birth. There is patchy, splash-like cutaneous pigmentation with whorls and splotches of pigment. It is associated with frequent ocular changes, absence or malformations of the teeth, and alopecia. The Naegeli type occurs in both males and females and appears after 2 years of age. There is a reticular type of pigmentation, sometimes associated with hypohidrosis, unhealthy and spotted teeth, and keratosis of palms and soles.

The ocular anomalies occur in about a quarter of cases of Bloch-Sulzberger syndrome. They include cataract, uveitis, blue sclerae, conjunctival pigmentation, strabismus, nystagmus, papillitis, optic atrophy, metastatic ophthalmitis, pseudoglioma, retrolental fibroplasia, phthisis bulbi, and microphthalmos.

Case report

The patient was a female born on 14 April 1962 at full term by normal delivery with a birth weight of 6 lb 12 oz (3060 g). The pregnancy was uneventful and the mother did not receive any medication during pregnancy. The patient has 4 siblings and they are all healthy. At birth she was noticed to have reddened skin and blisters on legs and arms, and when 3 days old she was admitted to hospital with erythema and bullous eruptions involving scalp, ears, hard palate, forearms, buttocks, thighs, knees, and calves. By 9 days of age the lesions had extended to the chest, and the patient became very toxic. The general condition started improving in the next 3 weeks with nursing care. She was given several courses of antibiotics, as she was very susceptible to upper respiratory infections. The condition stabilised by 3 months of age, and the lesions started becoming pigmented (Fig. 1). It was clinically diagnosed as epidermolysis bullosa, but the diagnosis was changed to IP as pigmentation started. At the age of 4 months skin biopsy established the diagnosis of IP.

At present the patient has classical bizarre whorls and streaks of pigmentation on the trunk and the left groin (Fig. 2). She is thinly built, with diffuse alopecia and very sparse hairs on the scalp. She has marked dental anomalies, having only a few pegged teeth.

OCULAR HISTORY

In October 1973 she was found to have defective visual acuity in the right eye during a routine school medical examination. Her visual acuity was 6/9 in the right eye and 6/5 in the left eye. The right vision improved to 6/5 with a small myopic correction. In April 1976 fundus changes were noticed in the right eye, and she was referred to the eye department of York District Hospital. She had no ocular symptoms.

On examination she was orthophoric and the

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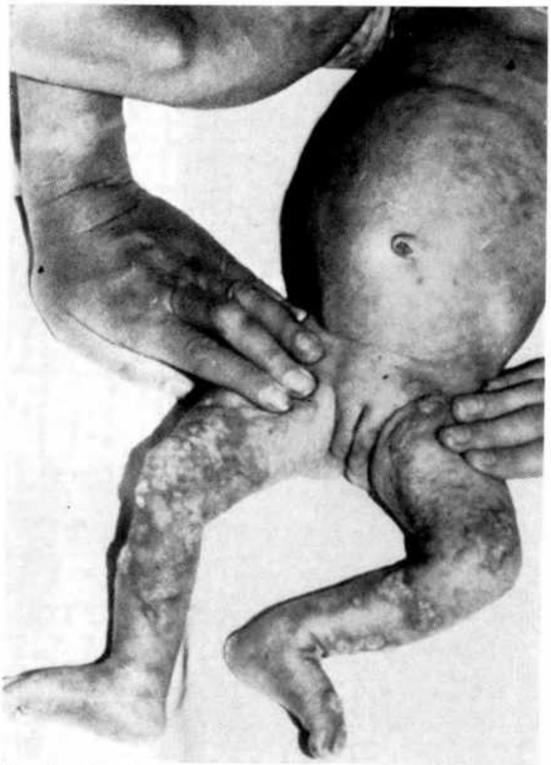

Fig. 1 *Skin lesions at 3 months of age. Bullous eruptions on lower limbs and chest which have started becoming pigmented.*

anterior segments were normal. Her visual acuity was 6/5 in the left eye and 6/18 in the right eye, improving to 6/9 with -0·75 D sphere. The left fundus was normal. The right fundus was seen through clear media. There were a few microaneurysms temporal to the macula. A venule just temporal to the macula and arising from the inferior temporal vein was slightly elevated from the retinal plane. There was some preretinal fibrosis in this area (Fig. 3). In the upper temporal equatorial region there was extensive preretinal fibrosis and retinitis proliferans (Fig. 4). The other areas of the fundus showed no gross abnormality. Her visual field was full in the left eye, but the right peripheral field showed lower nasal loss consistent with the changes in the temporal fundus.

Fluorescein angiography of the right eye was done. It confirmed microaneurysms in the macular area connected to the raised venule (Fig. 5). Fluorescence persisted in the microaneurysms for more than 5 minutes, but there was no leakage from these or from the venule. The temporal retinitis proliferans rapidly filled with fluorescein (Fig. 6) and gave rise to profuse leakage of dye, which persisted for more than 10 minutes.

Discussion

More than 200 cases of IP have been reported since its first description by Bloch in 1926. Most of the children are full-term normal deliveries. There is no definite hereditary pattern, though some hereditary cases have been reported—for example, it has been described in a mother and her 2 daughters (Jackson and Nigam, 1962). Sulzberger (1938) described a case whose mother, sister, and niece suffered in

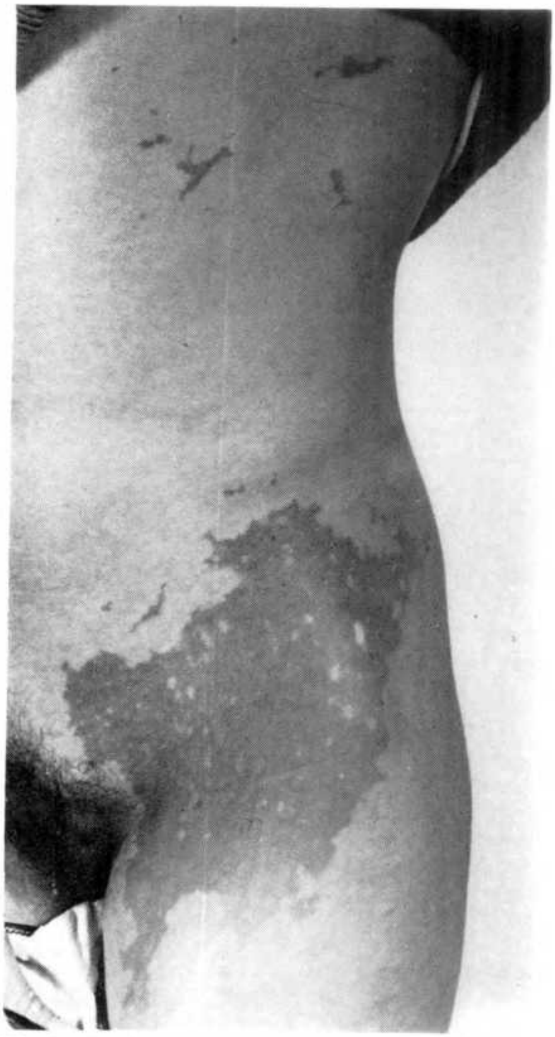

Fig. 2 *Skin lesions at 15 years of age. Bizarre whorls and streaks of pigmentation on the trunk and the left groin*

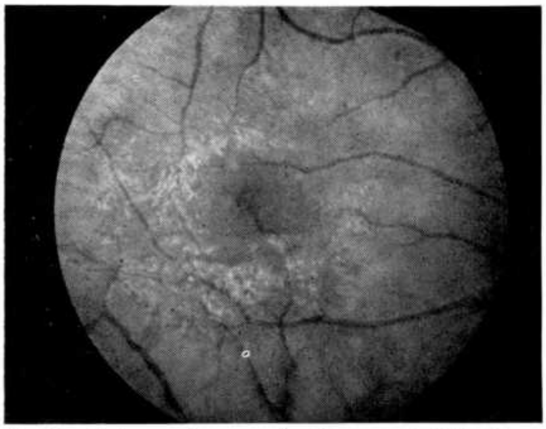

Fig. 3 *Right macular area showing preretinal fibrosis. A venule just temporal to the macula and arising from the inferior temporal vein is elevated from the retinal plane*

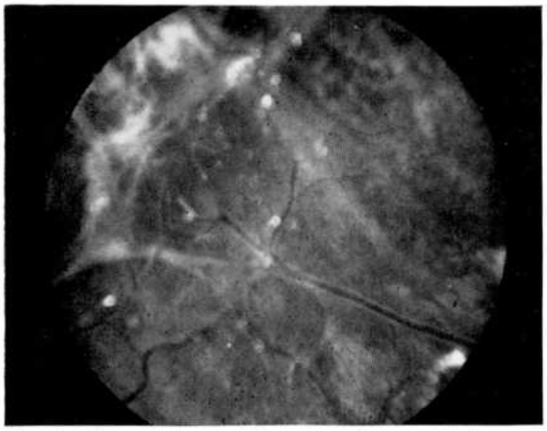

Fig. 4 *The upper temporal equatorial area of right fundus showing preretinal fibrosis and retinitis proliferans*

varying degrees from some congenital ectodermal anomalies. There is no family history of ectodermal anomaly in our case. There is a striking sex predilection, with girls being affected at a ratio of 20 to 1.

The term incontinentia pigmenti was first used by Bloch in 1926 because on histological examination he observed abnormalities of the pigmented cells of the epithelium which were thought to be 'incontinent' of melanin. The pigment is not retained by melanoblasts but drops into the corium and accumulates in the chromatophores instead of being desquamated upwards normally. The hyperpigmentation seen clinically is due to chromatophores heavily laden with melanin and situated within the upper and middle cutis. Electron microscopic examination of pigment in one case (Mensheha-Manhert *et al.*, 1975) showed mostly mature and some immature melanin granules and more lipofuscin than would be expected normally. The microscopic picture is not diagnostic of the condition (Haber, 1952). Similar histological appearances also occur in lichen planus, lupus erythematosis, Civatte's poikiloderma, Jacobi's poikiloderma, and Riehl's melanosis. However, the peculiar and characteristic clinical pattern of pigmentation is typical of the Bloch-Sulzberger syndrome.

The primary skin condition is present at birth or develops soon afterwards. It appears to be a macular or diffuse erythema which is characteristically associated with lichenoid papules and bullae arranged irregularly or in stripes. These bullae are

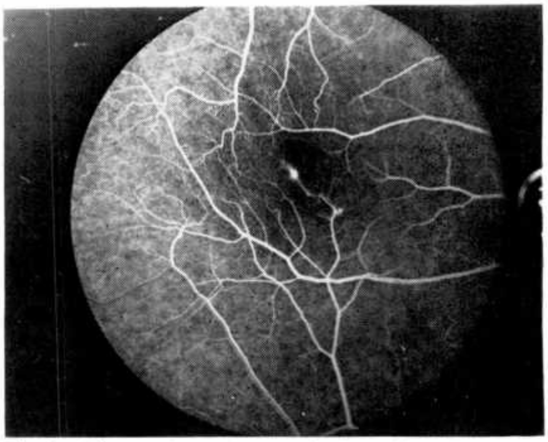

Fig. 5 *Fluorescein angiogram showing microaneurysms connected to the raised venule temporal to the right macula*

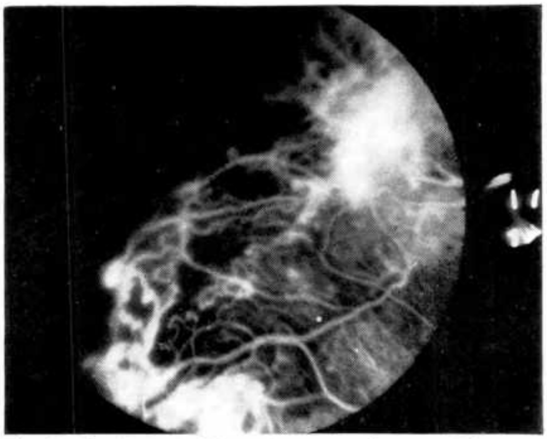

Fig. 6 *Retinitis proliferans in temporal equatorial region rapidly fills up with fluorescein*

liable to rupture and may lead to oozing and crusting. This stage is soon replaced by typical skin pigmentation. The pigmentary stage persists for a number of years, after which the pigment tends to disappear spontaneously.

Abnormalities of hairs and dentition are associated features of IP and they were both present in our case. In Bloch-Sulzberger syndrome there may be alopecia at the vertex with atrophy of skin in this area. The hairs in such areas are short and coarse. Delayed appearance of teeth of poor quality is often found in these patients. Variation in shape may also occur, as conical or irregular configurations. Total failure of tooth bud development has also been described.

Eye abnormalities have been noted in one-quarter to one-third of patients with this disease. Both anterior and posterior segment changes may occur. The anterior segment changes include cataract, uveitis, and blue sclerae. Pigmentation of the bulbar conjunctiva in the region of interpalpebral aperture has been described (McCrary and Smith, 1968), which histologically resembled the skin pigments. Nystagmus, strabismus, myopia, microphthalmos, and phthisis bulbi have also been described. A number of cases of IP have been reported with associated posterior segment changes which include optic atrophy (Carney, 1951; Lapiere, 1951), papillitis (Kuhling, 1949), persistent hyperplastic primary vitreous, metastatic ophthalmitis (Kawamura, 1954; Scott and others, 1955). ablatio falciformis, retrolental fibroplasia with or without pseudoglioma, retinal dysplasia (Findlay, 1952; Cole and Cole, 1959; Jones, 1966; Mensheha-Manhert and others, 1975; Miller and Anderson, 1966; Zweifach, 1966). About one-third of the ocular defects involve a mass in the posterior chamber. The retinal dysplasia and associated retinal detachment seen in IP may be secondary to the underlying abnormalities of retinal pigment epithelium, which in turn may reasonably be considered an expression of the underlying disorder of pigmentation.

Abnormal retinal pigmentation was described by Fischbein *et al.* (1972) in the form of small patches of depigmentation and pigment variegation scattered diffusely throughout the fundi. McCrary and Smith (1968) found patchy mottling of pigment in the midzone of the fundus in both eyes of a patient. This pigment proliferation and loss appear similar to the pattern of skin changes. Both these authors also performed fluorescein angiography in their patients, which showed bright fluorescence in the depigmented patches due to choroidal flush.

Findlay (1952) described a case with oedema of the posterior pole. All the retinal blood vessels and the whole choroidal bed were grossly dilated with several areas of punctate haemorrhages. Jensen (1956) reported a girl with a large oblique whitish membrane-like formation proliferating into the vitreous with vascularised processes to the retina. Its posterior portion concealed the optic disc. The adjacent retinal zone was slightly depigmented, while the peripheral retina showed diffuse dense pigmentation. In addition there were 2 small, well-defined retinal haemorrhages.

Lieb and Guerry (1958) described a case of exudative chorioretinitis associated with IP in a 4-week-old girl. The right fundus showed engorgement of the superior and inferior temporal veins. Temporal to the macula one branch of inferior temporal vein was markedly tortuous and engorged, resembling a corkscrew in configuration. The superior temporal vein showed multiple divisions resembling a pannus-like vascularisation. The whole temporal retina was oedematous, especially in the area of neovascularisation. In the left fundus the macular area showed extensive oedema and corkscrew vessels.

The fundus changes observed in our case have not previously been described in IP. Microaneurysms in the macular area were not reported in the earlier cases. The case reported by Lieb and Guerry (1958), like our case, also showed an abnormal branch of the inferior temporal vein temporal to the macula. The venule was elevated with some preretinal fibrosis, which formed a circinate pattern around the macular area. It did not show any leakage on fluorescein angiography. There was slight pigmentary disturbance in the macular area but no retinal oedema and no retinal haemorrhages. There were fine exudates in a fan shape between the macula and the retinitis proliferans temporally.

Although a number of cases of retinal dysplasia and retinal detachment have been reported, only 1 case (Jensen, 1956) showed connective tissue proliferation projecting into the vitreous. The patient described here has definite retinitis proliferans circumferentially in the equatorial region. There was sheathing along the superior temporal vessels and their branches, which on the temporal side became continuous with the retinitis proliferans. There was abnormal branching of the superior temporal vessels in the region of the retinitis proliferans. The retinitis proliferans showed marked leakage of fluorescein. The retinal changes were limited to the right eye. The fundus picture has not changed much in the past 1½ years under observation.

References

Bloch, B. (1926). Eigentümliche bisher nicht beschreibene Pigmentaffektion (incontinentia pigmenti). *Schweizerische-medizinische Wochenschrift*, 7, 404–405.

Carney, R. G. (1951). Incontinentia pigmenti—a report of five cases and review of literature. *Archives of Dermatology and Syphilology*, **64**, 126–135.

Cole, J. G., and Cole, H. G. (1959). Incontinentia pigmenti—associated with changes in the posterior chamber of the eye. *American Journal of Ophthalmology*, **47**, 321–331.

Findlay, G. H. (1952). On the pathogenesis of incontinentia pigmenti—with observation on an associated eye disturbance resembling retrolental fibroplasia. *British Journal of Dermatology*, **64**, 141–146.

Fischbein, F. I., Schub, M., and Lesko, W. S. (1972). Incontinentia pigmenti, pheochromocytoma and ocular abnormalities. *American Journal of Ophthalmology*, **73**, 961–964.

Haber, H. (1952). The Bloch-Sulzberger syndrome (incontinentia pigmenti). *British Journal of Dermatology*, **64**, 129–140.

Jackson, R., and Nigam, S. (1962). Incontinentia pigmenti—a report of three cases in one family. *Pediatrics*, **30**, 433–442.

Jensen, V. A. (1956). Incontinentia pigmenti (Bloch-Sulzberger syndrome) associated with proliferative eyeground changes and positive toxoplasmosis reaction. *Acta Psychiatrica Scandinavica*, **31**, 197–202.

Jones, S. T. (1966). Retrolental membrane associated with Bloch-Sulzberger syndrome (incontinentia pigmenti). *American Journal of Ophthalmology*, **62**, 330–334.

Kawamura (1954). Cited by Miller, R. J., and Anderson, R. E. Incontinentia pigmenti in Japan. *Archives of Dermatology and Syphilology*, **69**, 667.

Kuhling, F. (1949). Cited by Lieb, W. A., and Guerry, D. *Incontinentia Pigmenti*. Dissertation, Wurzburg.

Lapiere, S. (1951). Cited by Lieb, W. A., and Guerry, D. Incontinentia Pigmenti. *Archives Belges de Dermatologie et de Syphiligraphy*, **7**, 156.

Lieb, W. A., and Guerry, D. (1958). Fundus changes in incontinentia pigmenti. *American Journal of Ophthalmology*, **45**, 265–271.

McCrary, J. A., and Smith, J. L. (1968). Conjunctival and retinal incontinentia pigmenti. *Archives of Ophthalmology*, **79**, 417–422.

Mensheha-Manhert, O., Rodrignes, M. M., Shields, J. A., Shannon, G. M., and Mirabelli, R. P. (1975). Retinal pigment epithelium in incontinentia pigmenti. *American Journal of Ophthalmology*, **79**, 571–577.

Miller, R. J., and Anderson, R. E. (1966). A retrolental mass in incontinentia pigmenti—case report and review of literature. *Survey of Ophthalmology*, **11**, 41–46.

Scott, J. G., Friedmann, A. I., Chitters, M., and Pepler, W. I. (1955). Ocular changes in the Bloch-Sulzberger syndrome (incontinentia pigmenti). *British Journal of Ophthalmology*, **39**, 276–282.

Sulzberger, M. B., Frazer, J. F., and Hunter, L. (1938). Incontinentia pigmenti. *Archives of Dermatology and Syphilology*, **38**, 57.

Zweifach, P. H. (1966). Incontinentia pigmenti: its association with retinal dysplasia. *American Journal of Ophthalmology*, **62**, 716–722.

British Journal of Ophthalmology, 1978, **62**, 627–643

Contractile proteins in retinal endothelium and other non-muscle tissues of the eye

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SUMMARY The present study is the first investigation to demonstrate, by employing the combined approach of immunological and electron microscopic methods, the presence of actin-like contractile proteins in the mammalian retina, the corneal epithelium and endothelium, the iris, and the ciliary body, and to confirm their presence in lens epithelium. This is also the first report to demonstrate by these methods the presence of microfilaments and intermediate filaments in retinal vascular endothelium. Since we have shown that actin filaments are especially abundant in immature retinal endothelial cells, the question of their function arises, and we have discussed their possible relevance to the closure of immature retinal vessels when exposed to hyperoxia.

The cause of the peculiar sensitivity of immature mammalian retinal vessels to hyperoxia, which react by severe constriction leading eventually to their complete and irreversible closure (Ashton *et al.*, 1954), remains unknown. One obvious explanation would be that for some reason immature vessels are more actively contractile than those of the adult, but this would be surprising since the latter possess a fully developed musculature, whereas the simple endothelial tubes of growing vessels still lack this differentiation. Curiously, the less mature the developing vasculature the greater the sensitivity to oxygen, and in seeking an explanation in the past it has been difficult to imagine upon what cellular or subcellular component any vasoconstrictor might act.

Indeed, the question whether endothelial cells are alone capable of contraction had been a matter of controversy for over a century. In an extensive review of the subject Wiedeman (1963) concluded that the accumulated evidence was overwhelmingly in favour of capillaries being non-contractile. Filaments have, however, been repeatedly observed in the cytoplasm of endothelial cells of various mammalian tissues, and it had been suggested that these might be contractile, but Rhodin (1967), although regarding the endothelial filaments as indistinguishable from myofilaments of smooth muscle, felt unable in the absence of experimental proof to conclude that this necessarily implied endothelial contractibility.

Moreover, Cecio (1967), in an ultrastructural study of capillary endothelium in the rat, believed that the lack of periodicity in the cytofilaments and the absence of nervous connections actually excluded the possible active contractility of the cells and that the filaments had only a supportive and elastic function. Becker and Murphy (1969) have since demonstrated by immunofluorescence the presence of the contractile protein actomyosin in human cardiac endothelial cells, a finding in harmony with the contractile hypothesis. In the same year Majno *et al.* (1969) published a full account of their work showing the contractile power of endothelial cells in response to histamine-type mediators.

In view of this evidence we thought it would be of interest to examine immature and mature retinal endothelium for the presence of contractile protein antigens. For the demonstration of actin filaments in situ 2 techniques are currently in vogue. One method relies on the capacity of actin molecules to form 'arrow head' complexes, as seen electron microscopically, when incubated with myosin subfragment-1 or heavy meromyosin (Goldman, 1975). The other, which is simpler, more versatile, and able to localise not only actin but other intracellular contractile proteins, depends on the property of smooth muscle antibody (SMA), contained either in pathological human sera or, as pure actin antibody, in the sera of immunised animals, to react with cells and tissues where the antibody-combining sites correspond to those in which microfilaments have been demonstrated ultrastructurally (Holborow *et al.*, 1975; Trenchev *et al.*, 1976). The present communication is concerned with the latter

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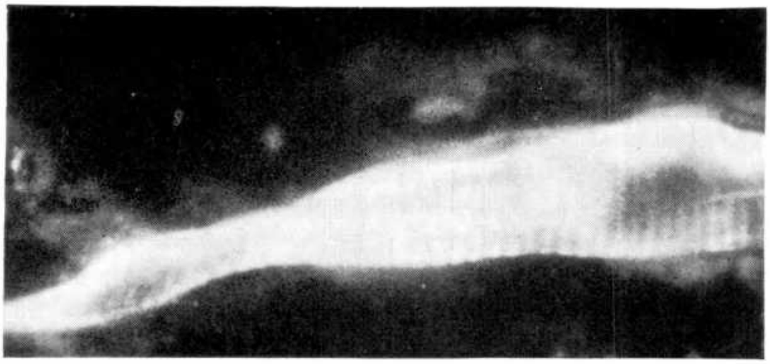
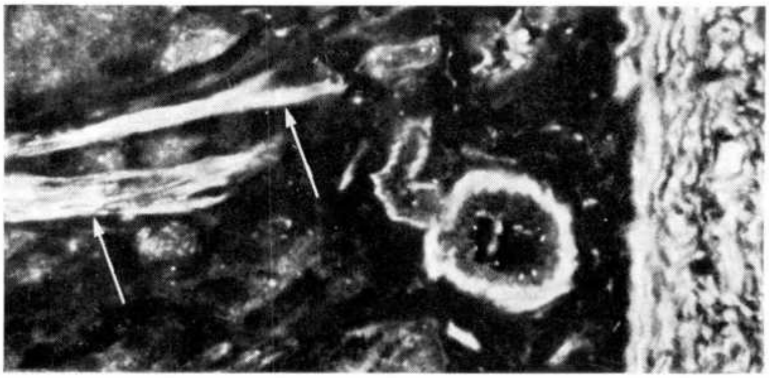


Fig. 1 *Indirect immunofluorescence test on rat skeletal muscle. The smooth muscle antibody reacts with actin in the muscle fibre to produce bright fluorescence of the 'I' band. Unfixed cryostat section* (×1600)

Fig. 2 *Cryostat section of rat stomach treated with smooth muscle antibody and fluorescein-labelled anti-immunoglobulin. The muscularis mucosa, the vessel wall, and the muscle fibres between the gastric glands (arrows) show brilliant fluorescence* (×960)



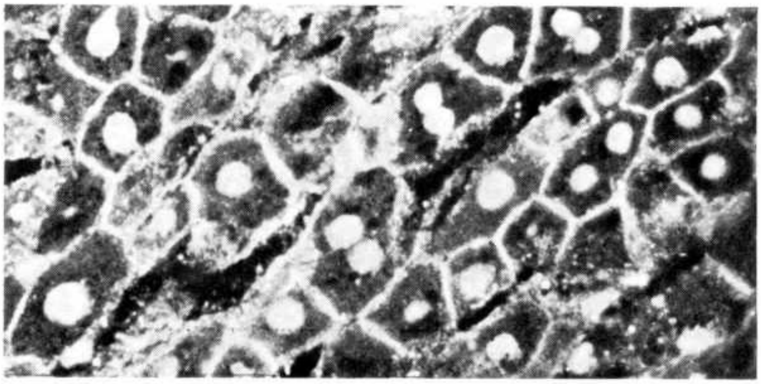


Fig. 3 *Cryostat section of a rat liver. Polygonal staining of the cell periphery is due to the presence of actin-like proteins. The section was consecutively treated with smooth muscle antibody and fluorescein-labelled immunoglobulin. The nuclear fluorescence is due to the presence of antinuclear antibody in the patient's serum* (×960)

technique for the immunological identification of actin and other contractile proteins in non-muscle tissues, and we report not only our observations on retinal endothelium but also our incidental findings in other ocular tissues.

Materials and methods

Blood from patients with chronic uveitis or intraocular melanoma which was found to contain high titres (that is, >1:160) of smooth muscle antibodies (SMA) (Rahi *et al.*, 1976), particularly against actin as judged by the standard criteria (Trenchev and Holborow, 1976), was used as the main source of antiserum for the localisation of actin-like proteins. However, the reactivity and the specificity of this serum were standardised against pure antiactin serum raised in rabbits (Holborow *et al.*, 1975; Trenchev and Holborow, 1976). Myosin was first extracted from smooth muscle homogenate of human uterus with various concentrations of KCl (pH 6·8). The remaining tissue was swollen in

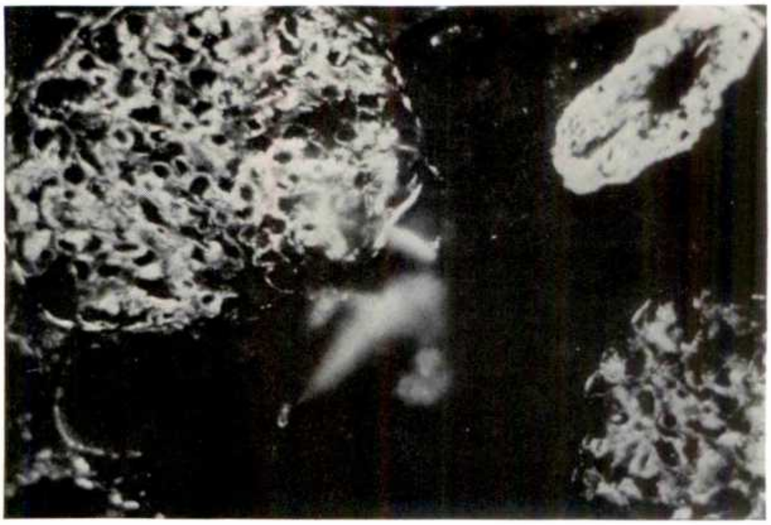


Fig. 4 (a) *Indirect immunofluorescence test on frozen section of a rat kidney. The patient's serum reacts with 2 glomeruli and an artery to produce bright fluorescence of the contractile elements* (× 640)

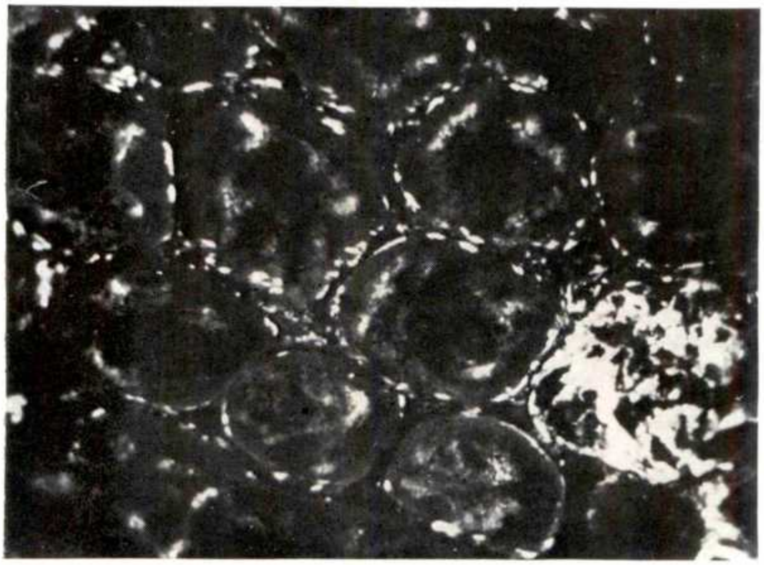


Fig. 4 (b) *Cryostat sections of a rat kidney treated in the same way with smooth muscle antibody. The peritubular fluorescence is probably due to the presence of actin-like proteins in basal processes of the tubular epithelium and muscle cells in the intertubular zone* (× 320)

0·01 M $NaHCO_3$, dried in acetone, and protein was extracted in deionised distilled water containing 2 mM-tris-HCl, 0·2 mM ATP, 0·5 mM mercaptoethanol, and 0·2 mM $CaCl_2$ (pH 8·2). The crude actin thus obtained was purified on Sephadex G200. Antiserum against actin was raised in rabbits by giving each rabbit a single injection of 1 mg protein emulsified with Freund's complete adjuvant. The rabbits were bled 3 weeks later and serum stored at −20°C in small aliquots.

STANDARDISATION PROCEDURE

Frozen sections of a composite block consisting of portions of liver, kidney, skeletal muscle, stomach, and salivary gland of a rat were used to demonstrate smooth muscle antibodies (especially against actin) in patients' sera and in sera obtained from immunised rabbits.

RETINAL ENDOTHELIUM AND OTHER OCULAR STRUCTURES

For this study the following preparations were employed: (1) Frozen sections of rat eyes; (2) vascular complexes from the retinae of (*a*) 9-day-old rabbits, (*b*) adult rabbits; (3) tissue cultures of retinal vascular complexes from (*a*) 9-day-old

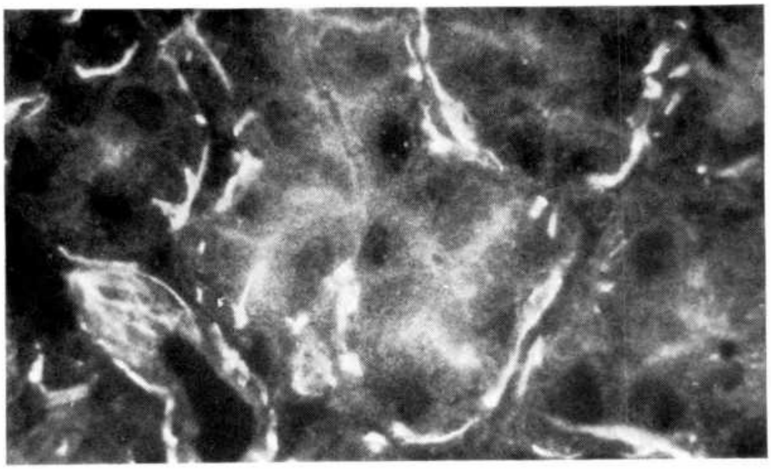


Fig. 5 *Myoepithelial cells in a rat parotid showing bright periglandular fluorescence in the presence of smooth muscle antibody. Indirect immunofluorescence test* (×640)

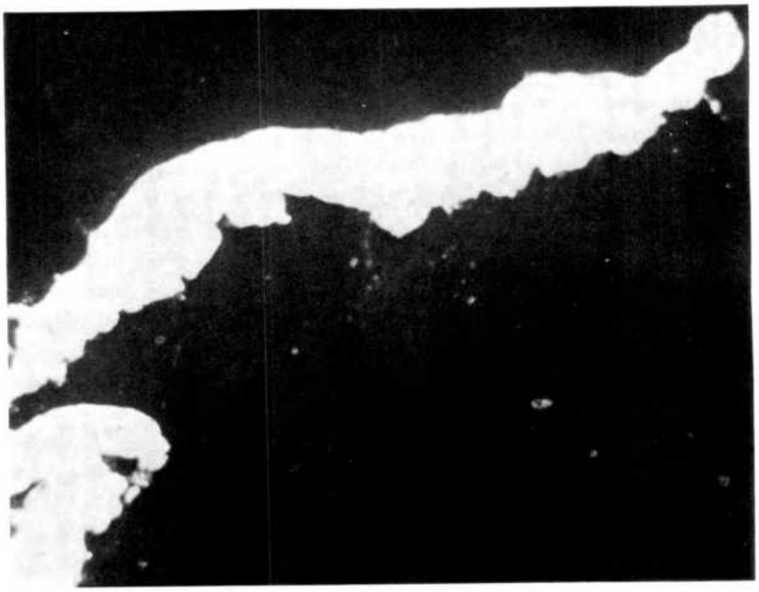


Fig. 6 *Cryostat section of a rat eye showing bright fluorescence of the iris and the ciliary body. The tissue was consecutively treated with antiactin serum and fluorescein-labelled anti-immunoglobulin* (×320)

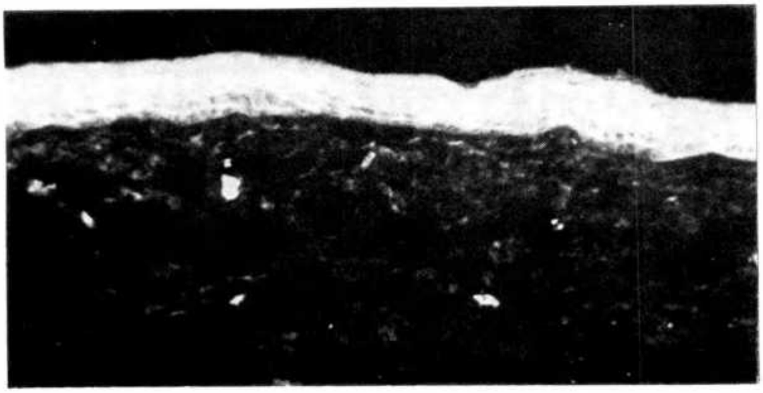


Fig. 7 *Indirect immunofluorescence test on rat eye. The antiactin serum reacts with the cytoplasm of the corneal epithelium to produce bright fluorescence of the contractile elements. Unfixed cryostat section* (×320)

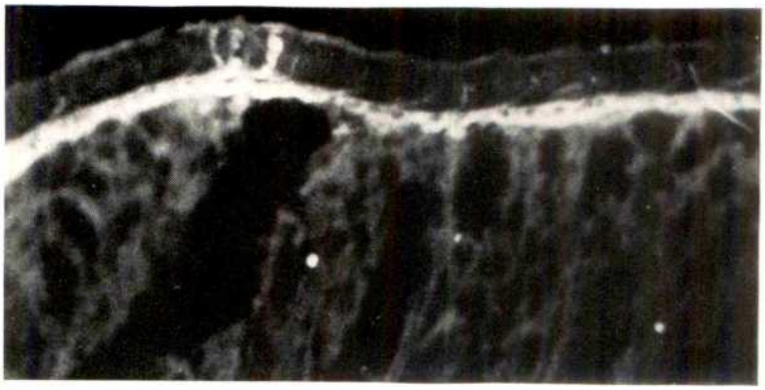


Fig. 8 *Cryostat section of a rat lens showing bright cytoplasmic fluorescence of the epithelium in the presence of anti-actin serum* (×320)

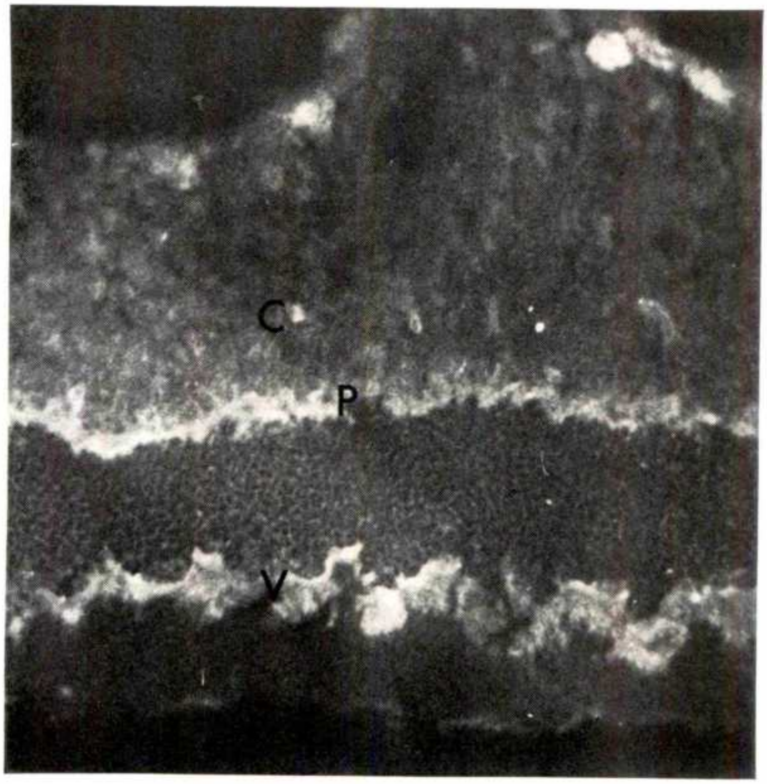


Fig. 9 *Cryostat section of rat retina showing bright fluorescence of retinal capillaries (C), the outer plexiform layer (P), and the inner segments of visual cells (V). The tissue was consecutively treated with smooth muscle antibody and fluorescein-labelled anti-immunoglobulin* (×320)

rabbits, (*b*) adult rabbits (Ashton 1961; Tripathi *et al.*, 1973).

IMMUNOFLUORESCENT TECHNIQUE

A standard method was followed using fluorescein-labelled antihuman and antirabbit immunoglobulins (Wellcome Laboratories). A Zeiss epifluorescence microscope equipped with fluorescein isothiocyanate (FITC) interference filter was used to examine the above specimens. Frozen sections of the composite block and rat eyes were air dried. The tissue-culture preparations were washed in isotonic saline and fixed in acetone.

ELECTRON MICROSCOPY

Cultures of rabbit retinal vascular complex, human lens epithelium, and rabbit corneal endothelium were grown on Melinex discs. Fixation was carried out by floating the Melinex discs, specimen side down, on 3% glutaraldehyde in cacodylate buffer pH 7·4 for 2 hours at room temperature in covered Petri dishes. They were then washed in sucrose

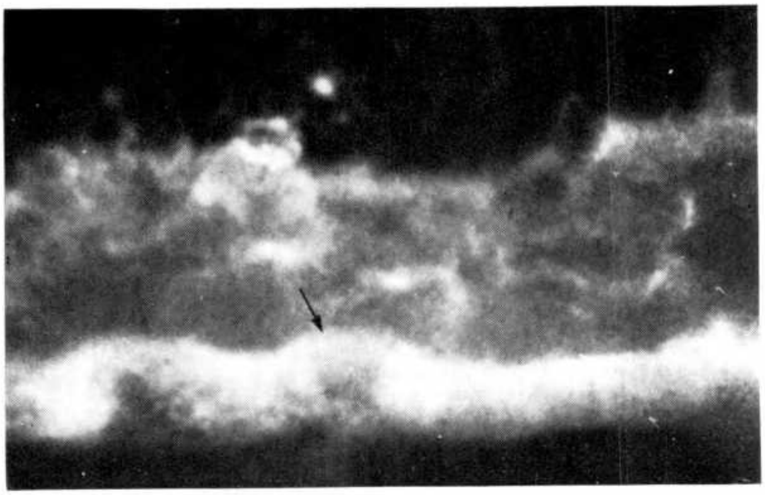
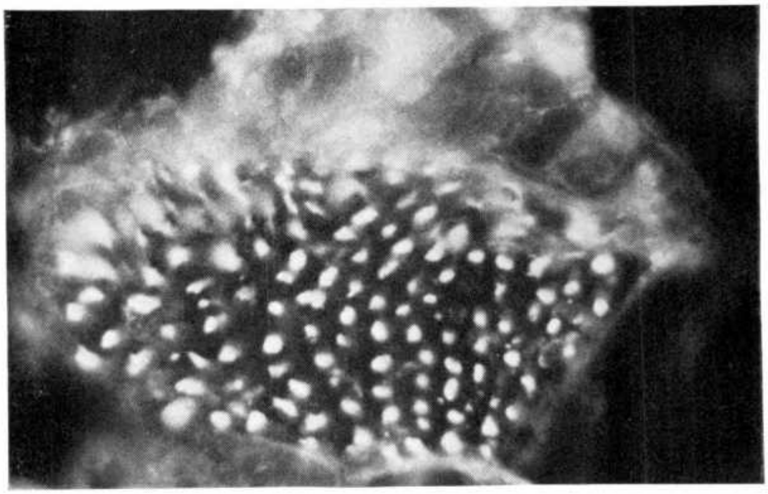


Fig. 10 *Indirect immunofluorescence test. The pigment epithelium of the retina (arrow) and the photoreceptor elements in the cryostat section of a rat eye show bright fluorescence in the presence of smooth muscle antibody* (× 960)

Fig. 11 *Nerve fibres in cryostat sections of an extraocular muscle showing bright fluorescence. The contractile elements in these fibres have reacted with smooth muscle antibody to produce a bright fluorescence after treatment with fluorescein-labelled antiglobulin* (× 960)



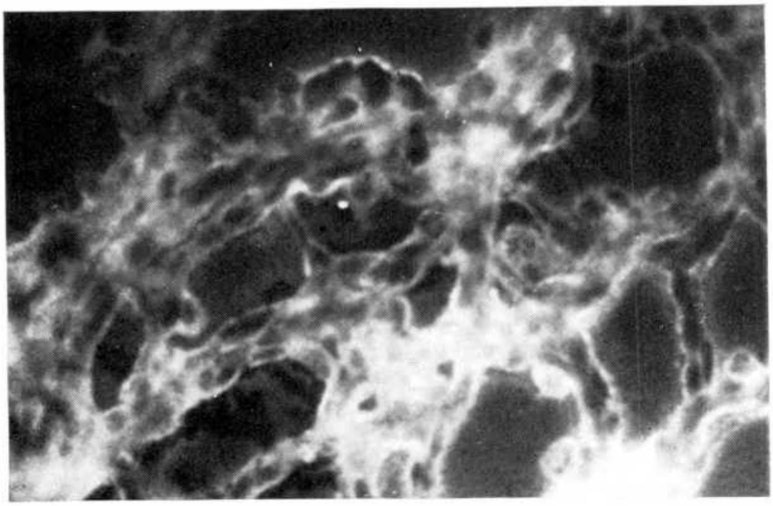


Fig. 12 (a) *Retinal vascular complex of 9-day-old rabbit stained directly after acetone fixation for the presence of smooth muscle protein. Note the mild to moderate fluorescence of the differentiating endothelial cells* (× 213)

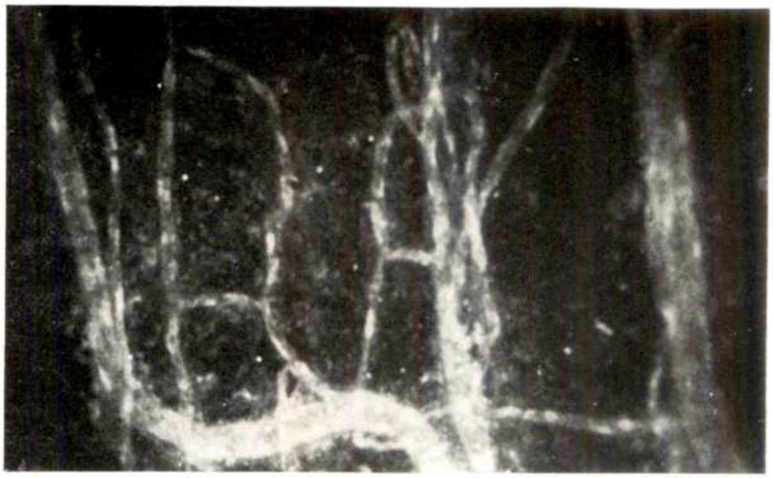


Fig. 12 (b) *Retinal vascular complex from an adult rabbit treated in the same way. The capillaries show only mild fluorescence. The large vessels which contain some smooth muscles are strongly fluorescent* (×213)

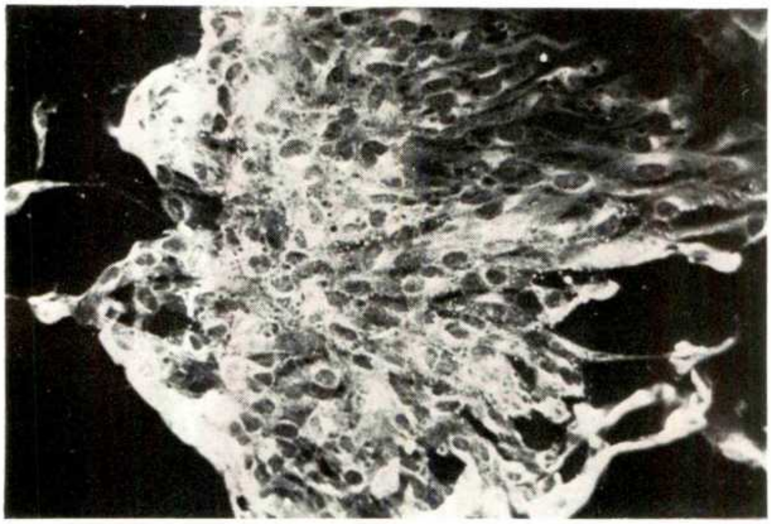


Fig. 13 *Acetone-fixed 7-day-old culture of retinal vascular complex from a 9-day-old rabbit. The endothelial cells show bright fluorescence in the presence of smooth muscle antibody* (×213)

buffer, with 2 changes (15 minutes each), followed by post-fixation in 1% isotonic OsO_4 in veronal acetate buffer for 1 hour. The cultures were washed in sucrose buffer for 15 minutes and dehydrated in ascending grades of ethanol. Excess Melinex was trimmed from the discs, and the resulting rectangles were transferred to sealed bottles for infiltration with Araldite epoxy resin. The specimens were finally embedded flat. When polymerised the Melinex was peeled off, exposing a monolayer of cells. Specimens of retinal vascular complex from adult and 9-day-old rabbits were also directly fixed in isotonic glutaraldehyde and similarly dehydrated and embedded in Araldite.

Sections were cut on a Huxley ultramicrotome using a glass knife. Semithin sections (0·5 to 1·0 μm) for light microscopy were stained with 1% toluidune blue. Thin sections (50 to 80 nm) were stained with alcoholic uranyl acetate and aqueous lead citrate for electron microscopy. Sections were examined with a JEOL 100C electron microscope.

Findings

IMMUNOFLUORESCENT STUDIES

Standardisation

The skeletal muscles showed specific fluorescence of actin containing 'I' bands (Fig. 1). In the sections of the stomach specific bright fluorescence of the muscularis mucosa, the vessel walls, and the smooth muscle fibres between the gastric glands was observed (Fig. 2). The hepatocytes showed a polygonal staining pattern in which the contractile elements in the cell periphery showed bright fluorescence

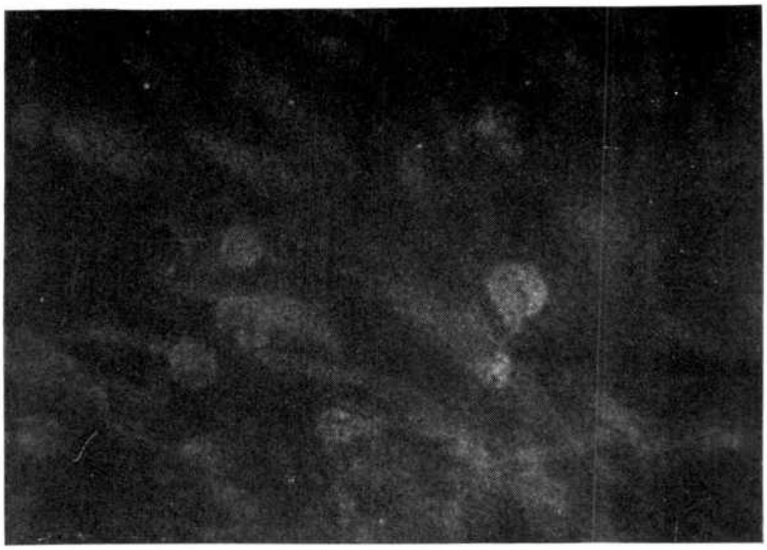


Fig. 14 *Acetone-fixed 7-day-old culture of retinal vascular complex from an adult rabbit. The elongated endothelial cells show only weak fluorescence. Round cells in the photograph are macrophages* (×320)

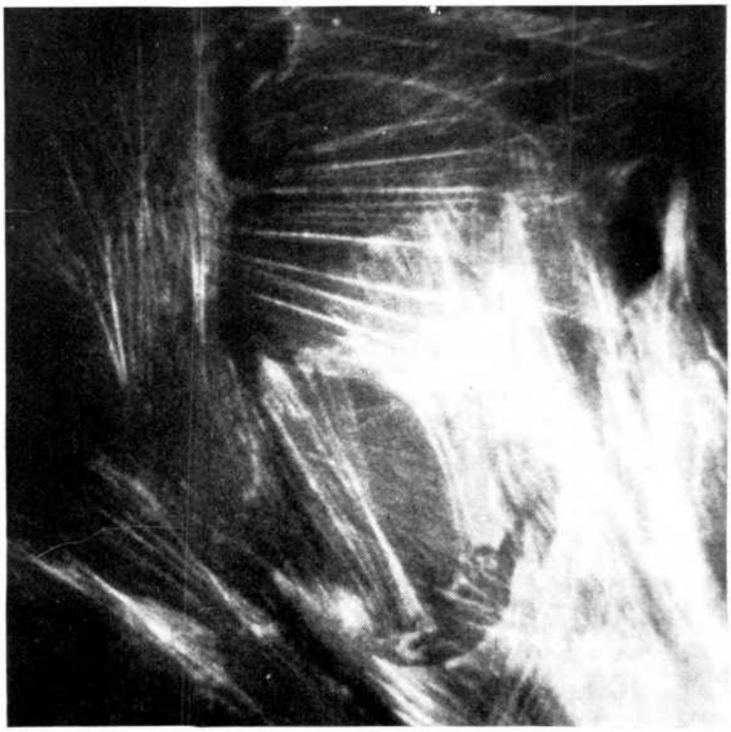


Fig. 15 *Acetone-fixed 14-day-old tissue culture preparation of retinal endothelial cells from a 9-day-old rabbit showing bright fluorescence of actin filaments, which were seen to converge on the plasma membrane of these cells. The preparations were consecutively stained with anti-actin serum and fluorescein-labelled anti-immunoglobulin* (×960)

(Fig. 3). In kidney sections characteristic fluorescence of the glomeruli and the peritubular tissues was observed (Figs. 4*a*, *b*). Sections of salivary gland showed strong fluorescence of myoepithelial cells (Fig. 5). All these features showed that the serum used in the present study was rich in antibodies to actin.

Contractile proteins in ocular tissues

As expected, the iris and the ciliary body, which are known to contain a large number of smooth muscle fibres, showed strong fluorescence when treated with either the patient's serum containing smooth muscle antibody or specific antiactin serum (Fig. 6). It was of interest, however, to note a similar

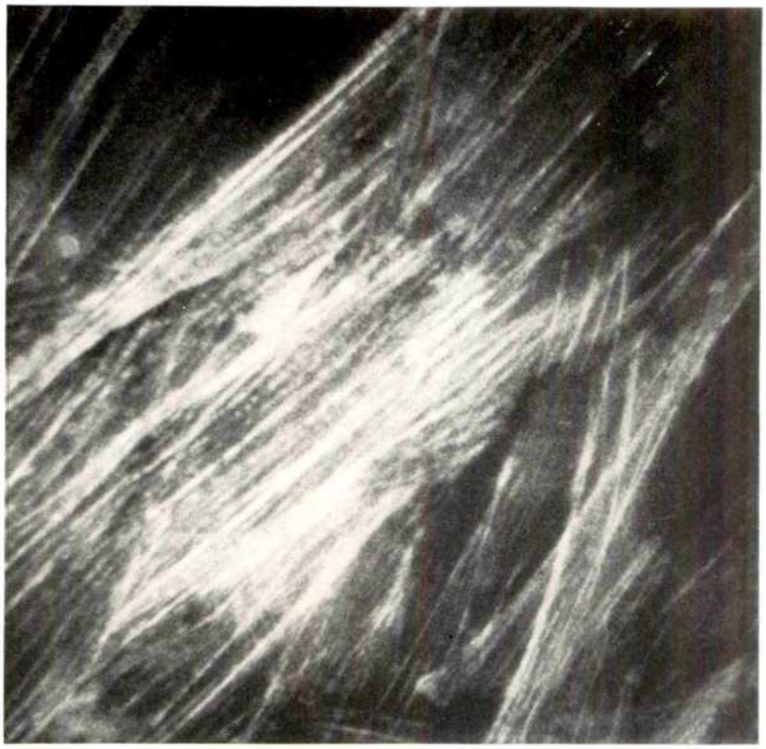


Fig. 16 *Acetone-fixed 14-day-old tissue culture preparation of retinal endothelial cells from a 9-day-old rabbit showing bright fluorescence of subcortical sheath of actin filaments (also called stress fibres) which run along the length of these cells. Indirect immunofluorescent test using antiactin serum* (× 960)

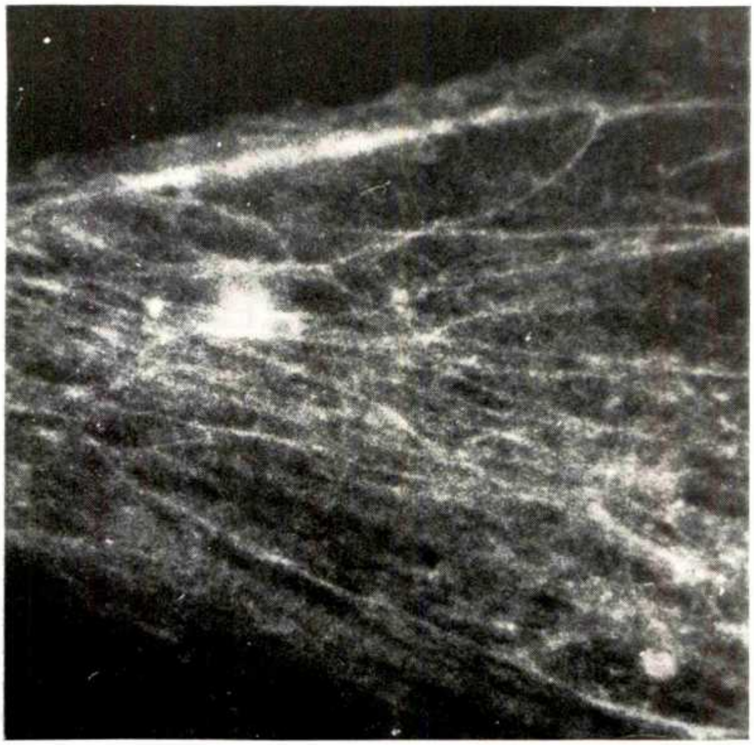


Fig. 17 *Acetone-fixed 14-day-old tissue culture preparation of retinal endothelial cell treated with patient's serum containing smooth muscle antibody. Note the loose fibrillar network in the cytoplasm of a cell indicating the presence of intermediate, 100Å (10-nm) filaments* (× 2400)

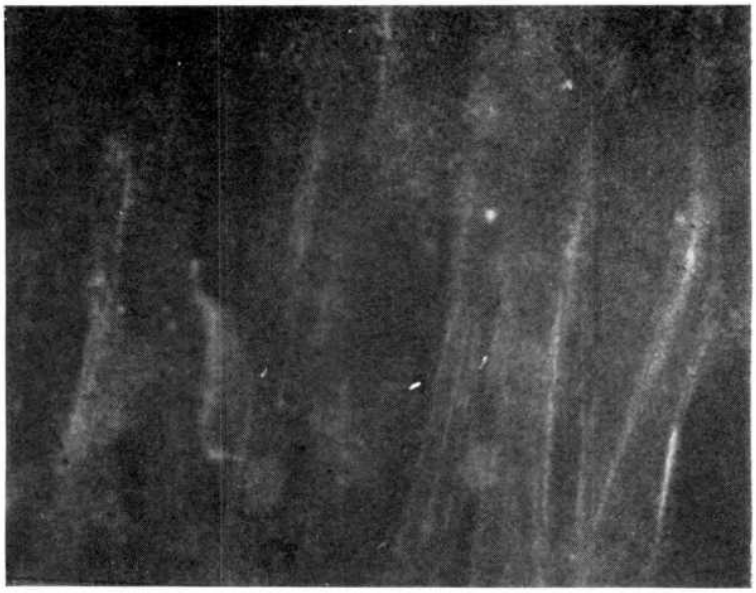


Fig. 18 *Acetone-fixed 14-day-old tissue culture preparation of retinal endothelial cells from an adult rabbit showing actin filaments in an immunofluorescent study. The filaments are not so numerous as in the endothelial cells from young rabbits shown in Figs. 15 and 16* (× 960)

bright fluorescence in the non-muscular tissues of the eye such as the corneal endothelium and epithelium (Fig. 7), the lens epithelium (Fig. 8), the outer plexiform layer of the retina and the inner segments of the photoreceptor cells (Fig. 9), and the pigment epithelium of the retina (Fig. 10), these findings suggesting a function-related preferential accumulation of contractile proteins in these intraocular structures. The nerve fibres supplying the extraocular muscles also gave a positive reaction with smooth muscle antibody (Fig. 11), probably due to the presence of contractile organelles in and around the nerve fibres related to axonal transport and the activity of the Schwann cells.

Retinal vascular complex

The retinal vascular complexes obtained from 9-day-old and adult rabbits and transferred directly on glass slides for immunofluorescent studies after acetone fixation showed only mild to moderate fluorescence of the endothelial cells (Figs. 12*a, b*).

Tissue culture studies

Acetone-fixed, 7-day-old culture preparations of retinal vascular complexes from 9-day-old rabbits showed strong fluorescence when treated with smooth muscle antibody (Fig. 13). Cultures of similar age from adult rabbits, however, showed only a weak fluorescence of the elongated endothelial cells (Fig. 14). This may be partly due to the fact that the endothelial cells from young animals, at least in the initial stages of tissue culture, appear larger in size.

Well established 14-day-old retinal endothelial cell cultures from young animals showed 3 types of filamentous cytoplasmic fluorescence. With antiactin serum either the filaments appeared to be converging to a point on the plasma membrane of the endothelial cells (Fig. 15) or the fibres formed thick bundles running across the length of the cells, which have been called 'actin cables' or 'stress fibres' (Fig. 16) in various other cell lines (Pollack *et al.*, 1975; Pollack and Rifkin, 1975; Wessels *et al.*, 1971).

Culture cells stained with patients' sera which in addition to antiactin antibody contained antibodies to other contractile proteins revealed a third type of arrangement, in which the cytoplasm showed a loose fibrillar network (Fig. 17), believed to consist of intermediate, 100-Å (10-nm), filaments. These are known by a variety of names in different tissues—for example, tonofilaments, neurofilaments, endothelial filaments—and contain a different contractile protein (Kurki *et al.*, 1977).

Tissue culture preparations which were several weeks old, or had stopped growing, or had been stored for a few days in the refrigerator before staining reacted differently with antiactin sera, showing instead of a filamentous staining only diffuse cytoplasmic fluorescence. This apparent loss of filamentous material was probably due to redistribution of actin molecules into a soluble non-aggregated form, as has been reported in virus-transformed cell lines (Pollack *et al.*, 1975). It is of interest that macrophages, which are normally present among the growing retinal endothelial cells, also showed a similar diffuse cytoplasmic

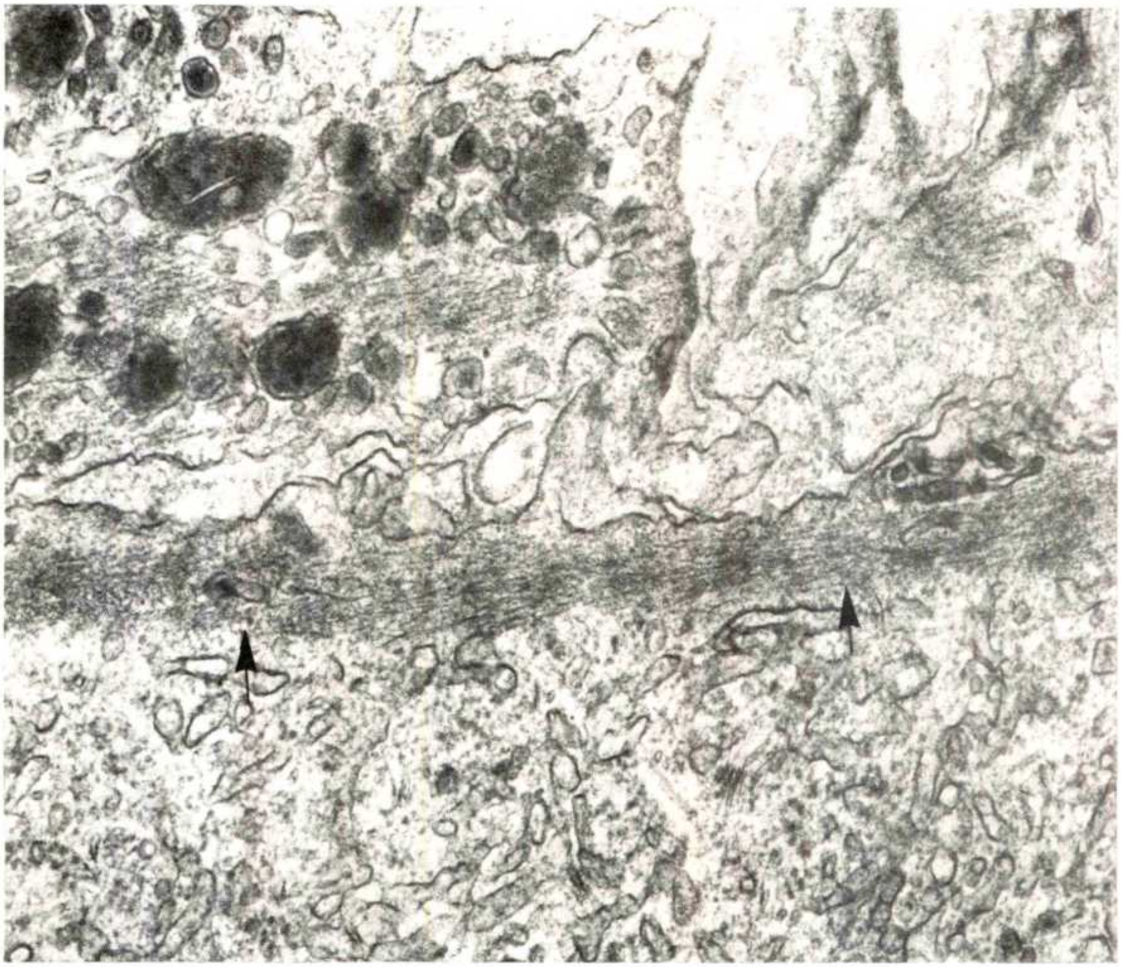


Fig. 19 *Pigment epithelial cell of rat. Numerous bundles of microfilaments, 50 to 75Å (5 to 7·5 nm) in diameter, are present in the cytoplasm (arrows). Electron microscopy,* × 52 000

fluorescence when treated with antiactin serum. These cells were, however, retracted and free floating.

Acetone-fixed 14-day-old tissue culture preparations of retinal endothelium from adult rabbits showed the presence of actin filaments, but their number was greatly reduced (Fig. 18). Whether this is due to a fundamental difference in the organisation of the cytoskeleton of the vascular endothelium in these 2 age groups or is simply a reflection of their *in vitro* growth potentials is uncertain, and a more detailed study is required for clarification.

ELECTRON MICROSCOPICAL STUDIES

Microfilaments in ocular tissues

Electron microscopical examination of rat retinal pigment epithelium (Fig. 19), human lens epithelium in tissue culture (Fig. 20), and rabbit corneal endothelium grown on Descemet's membrane showed the cytoplasmic network of microfilaments (Fig. 21) which provide the structural basis for the cytoplasmic fluorescence seen in the direct immunofluorescent study.

Retinal vascular complex in tissue culture

Electron microscopical examination of the tissue culture preparations of retinal vascular complexes from 9-day-old rabbits showed the presence of a large number of actin filaments, which appeared either as the cortical network (Fig. 22*a*) or as subcortical sheaths, the so-called stress fibres (Fig. 22*b*). Electron microscopical examination of the endothelial cells in the small blood vessels of

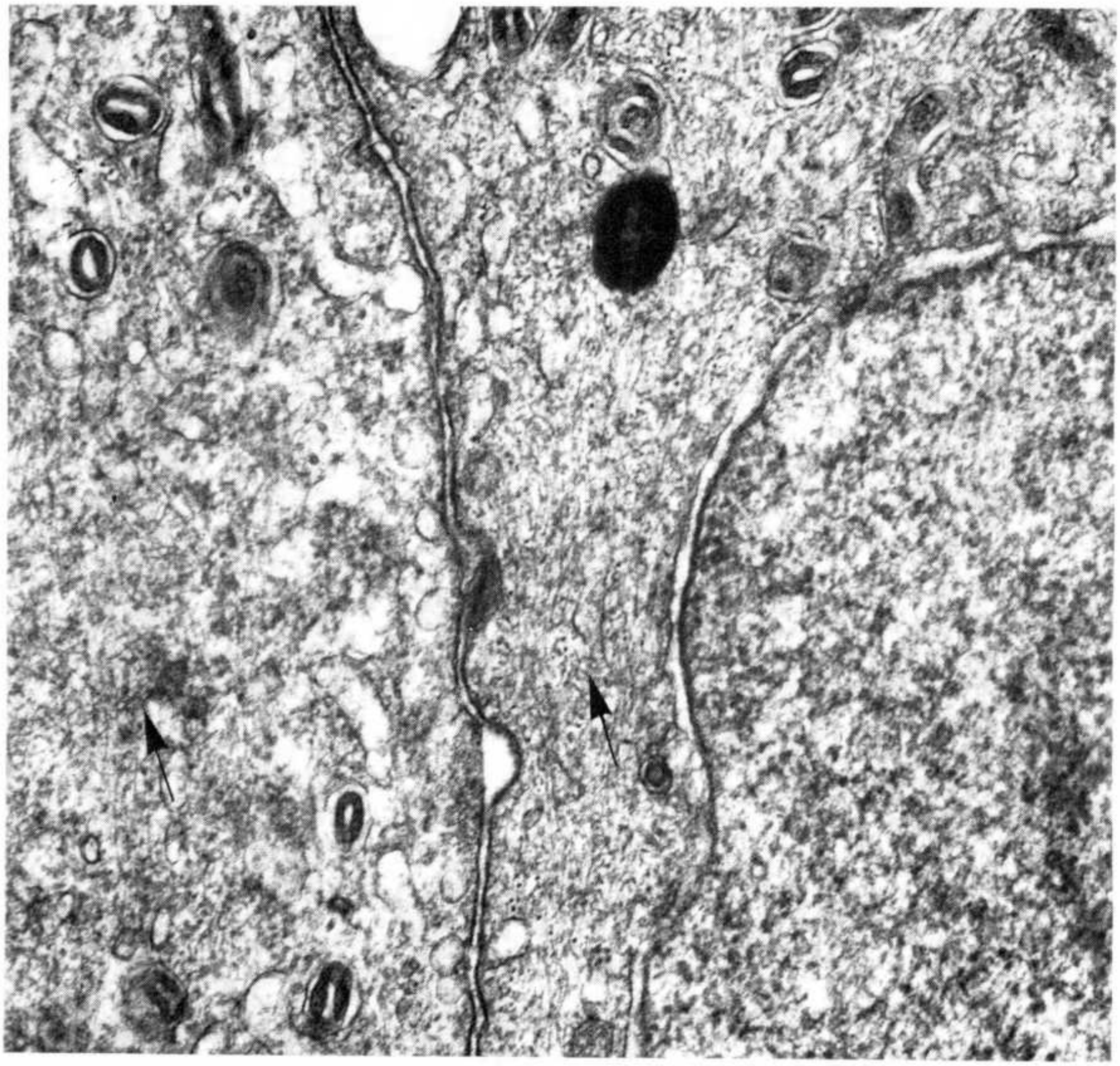


Fig. 20 *Human lens epithelium in tissue culture. Numerous microfilaments, 50 to 75Å (5 to 7·5 nm) in diameter, are present within the cytoplasm (arrows). Electron microscopy,* × 52 000

the retina directly removed from the enucleated eyes of 9-day-old and adult rabbits, however, did not show such a large number of microfilaments (Fig. 23), which suggests that the microfilaments appear in large numbers only at a certain stage of physiological activity such as growth, multiplication, and cytokinesis.

Discussion

The recent interest in actin and other contractile proteins stems from the findings that many mammalian cells contain these proteins in easily identifiable forms (Pollard and Weihing, 1974; Trenchev *et al.*, 1974). The content varies, however, in different types of normal, transformed, or neoplastic cells, and the morphological appearance of these intracellular proteins, particularly actin, depends on the physiological state of the cells and on pathological change (Pollack *et al.*, 1975; Gabbiani *et al.*, 1975).

The chief contractile elements of skeletal muscle are made up of a series of myosin and actin molecules. The myosin molecule is composed of 2 anti-

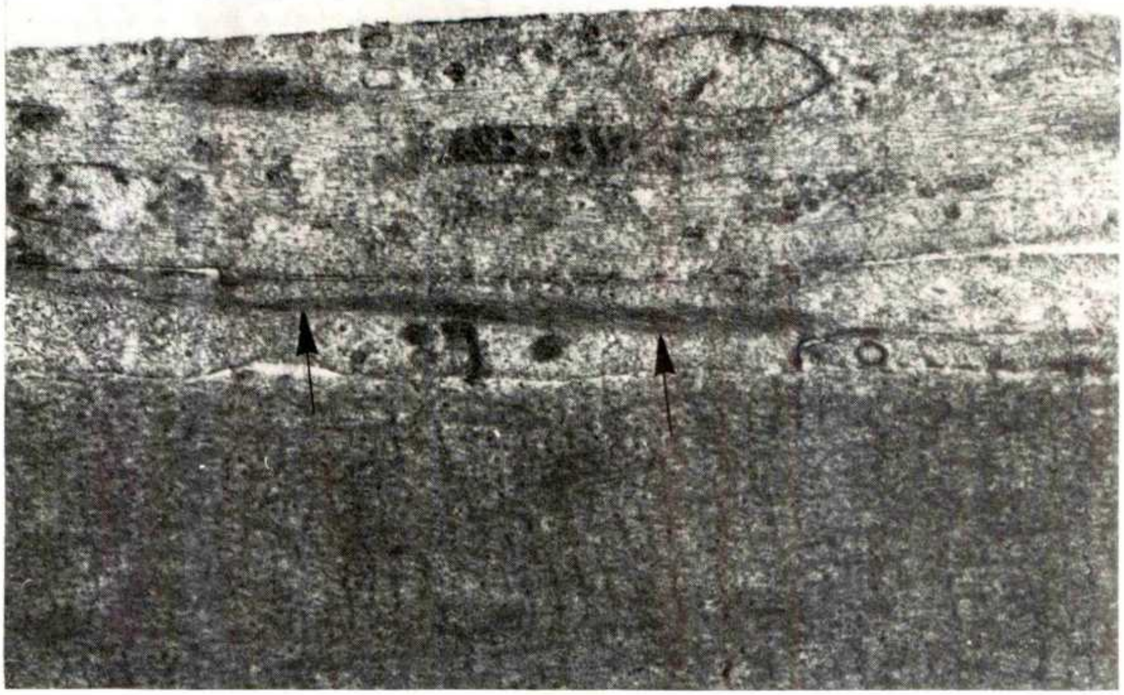


Fig. 21 *Rabbit corneal endothelial cells in tissue culture on Descemet's membrane. Numerous microfilaments lie in parallel in the longitudinal axis of the cell (arrows). Electron microscopy,* × 10 000

genically distinct components—light meromyosin and heavy meromyosin. The actin filaments on the other hand consist of double stranded F-actin helix, each containing several molecules of G-actin. The actin filaments also contain 2 additional antigenic proteins—tropomyosin and troponin.

In skeletal muscle cells the myosin and actin filaments interdigitate and show a banded arrangement (A and I bands), whereas in smooth muscle cells the actin and myosin filaments have no such spatial arrangement and lie at odd angles to each other, being mostly orientated in the longitudinal direction of the smooth muscle cell. Electron micrographs show typical actin filaments (50 to 75 Å (5 to 7·5 nm) in diameter), some of which are apparently attached by their tips to the smooth muscle cell membrane, thereby providing a method for mechanically coupling the contractile fibres to the cell surface.

Large fibres, 180 to 250 Å (18 to 25 nm) in diameter, forming microtubules and consisting of the contractile proteins α and β tubulin, are also seen in many cells, particularly in neural tissues, platelets, mast cells, and the mitotic spindle. Intermediate filaments, 100 Å (10 nm) in diameter, distinct from actin filaments and microtubules are also to be found in eukaryotic cells—markedly in epidermal and glial cells. They are regarded as cytoskeletal structures, and the protein of the filament has been named desmin or skeletin. Other proteins, such as filamin, spectrin, actinin, C-protein, and J-protein, have also been identified with various cellular structures.

Several activities of non-muscle cells depend on these specialised intracellular structures (i.e., actin microfilaments, microtubules, and intermediate filaments), and they are believed to be concerned with cell shape, mobility, and mitosis, with the tight junctions between cells and their adherence to glass surfaces in tissue culture, etc. (Lazarides, 1975; Feeney and Mixon, 1976).

OCULAR TISSUES IN GENERAL

The presence of the 3 major cytoplasmic filamentous structures in various tissues of the eye, such as the corneal epithelium, the lens epithelium, the various layers of the sensory retina, and the endothelium lining Schlemm's canal, has been known for some time (Kuwabara, 1965; 1968; Hogan *et al.*, 1971; Piatigorsky *et al.*, 1972; Rafferty and Esson, 1974; Grierson and Lee, 1975).

Actin-containing microfilaments have been

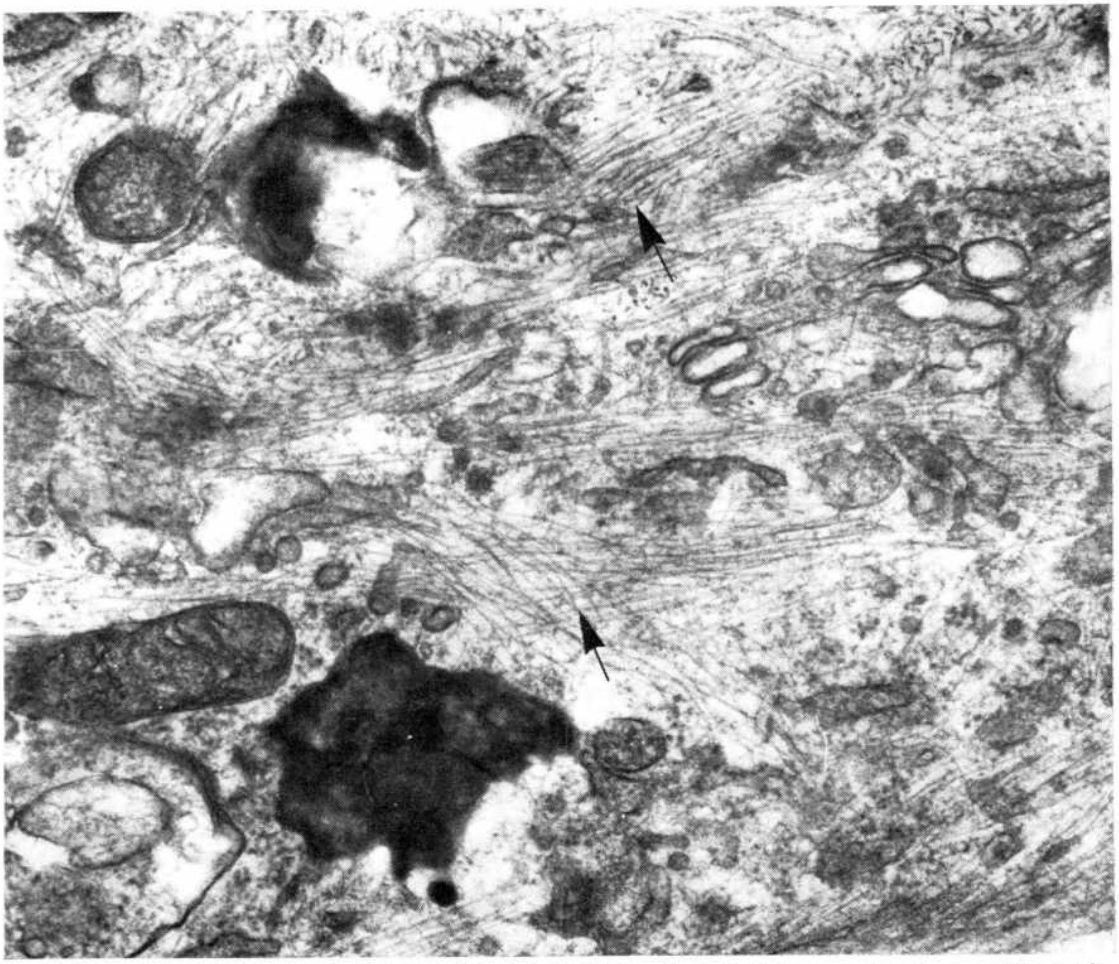


Fig. 22 (a) *A 7-day-old culture of retinal endothelium from a 9-day-old rabbit. Numerous microfilaments, 50 to 75Å (5 to 7·5 nm) in diameter, lie at odd angles to each other, but in the general longitudinal axis of the cell (arrows). Electron microscopy,* × 52 000

demonstrated in the retinal pigment epithelium and the corneal epithelium by the 'arrow-heading' technique (Gipson and Anderson, 1977), but there is only 1 ophthalmological study using immunofluorescent methods (Lonchampt *et al.,* 1976). These workers demonstrated microfilaments in rabbit lens epithelium using antiactin serum, and also microtubules reacting strongly to tubulin antibody: the filaments were also visualised by conventional electron microscopy.

Intermediate filaments in the form of tonofilaments, neurofilaments, glial filaments, and endothelial filaments are as familiar in the eye as elsewhere in the body (Hogan *et al.,* 1971), and both microtubules and actin filaments have been described in the retinal pigment epithelium of man and monkey (Burnside and Laties, 1976) and of the rat (Burnside, 1976).

The present study, however, is the first investigation to demonstrate, by employing the combined approach of immunological and electron microscopical methods, the presence of actin-like proteins in ocular tissues and to show their preferential disposition in the mammalian retina (that is, pigment epithelium, inner segments of visual cells, and the plexiform layers), the corneal epithelium and endothelium, the iris, and the ciliary body, and to confirm the previous report on the lens epithelium (Lonchampt *et al.,* 1976).

RETINAL VASCULAR COMPLEXES (RABBIT)

This is also the first report to demonstrate by these

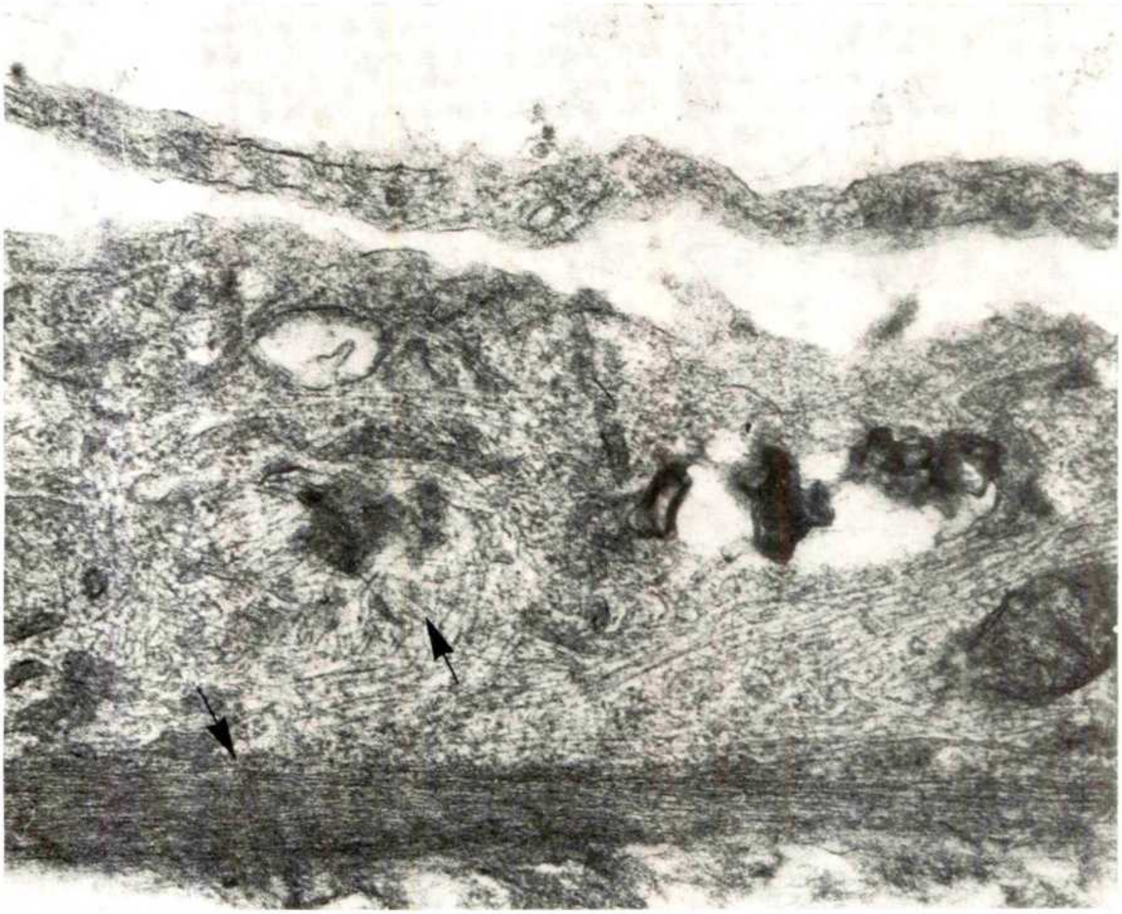


Fig. 22 (b) *Another cell from the same culture showing a subcortical 'actin cable' or 'stress fibre' (arrow) and other disorientated microfilaments (arrow). Electron microscopy,* × 52 000

methods the presence of microfilaments and intermediate filaments in the retinal vascular endothelium, although filaments have been previously described in pericytes (Ashton and Tripathi, 1977). Our findings that actin filaments are especially abundant in immature retinal endothelial cells raises the question of their function. Although the role of such filaments in muscles and in phagocytic cells is well documented, their precise role in vascular endothelium is unknown, but their presence at least suggests that these primitive cells are well equipped to contract when appropriately stimulated. That contraction of immature retinal vessels of the rabbit does occur as a result of oxygen exposure has been demonstrated in *in vivo* experiments (Ashton *et al.*, 1972; Tripathi *et al.*, 1974), and it would now seem reasonable to attribute at least the initial closure of the circulation to reactive contraction of these growing vasoformative cells. Moreover, the fact that we found actin microfilaments most evident in the more primitive cells would correspond to the greater reactivity to hyperoxia to be found in the ingrowing cells of the peripheral retinal complex as compared with the more mature vessels differentiating posteriorly. Such a reactive contraction to oxygen in the immature retina was suggested many years ago (Ashton *et al.*, 1954) when a few pilot experiments to test the possible effect of antagonism by vasodilators (for example, Priscol, CO_2) were carried out, but with negative results. It might now be rewarding to examine experimentally *in vivo* or *in vitro* the possible influence of substances known to cause disruption of microfilaments—for example, cytochalasin B (Rathke *et al.*, 1975).

To explain the comparative immunity to hyperoxia found in the adult retinal circulation, which has

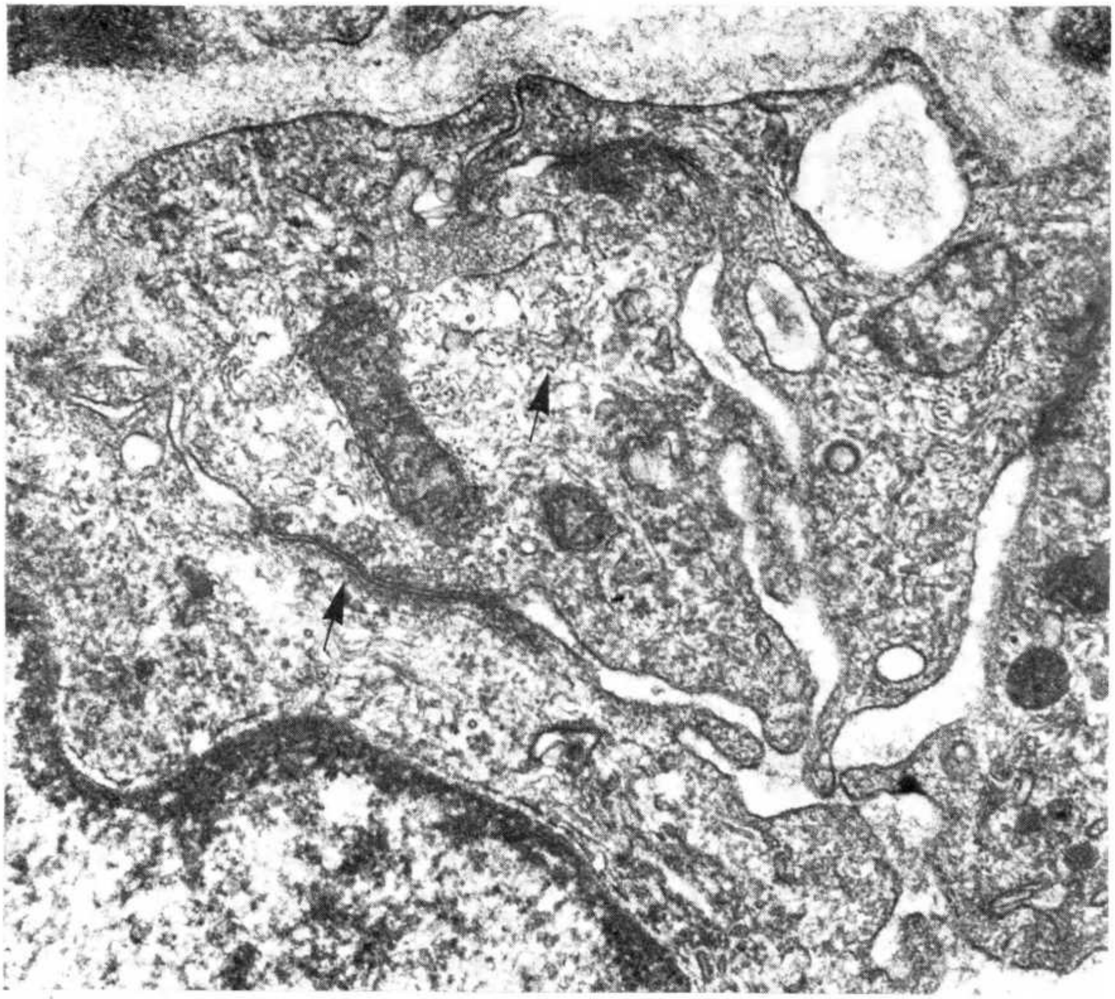


Fig. 23 *Developing retinal vessel from a 9-day-old rabbit. Microfilaments, 50 to 100Å (5 to 10 nm) in diameter, are present within the cytoplasm (arrows) but less prominent than in the corresponding cultured cell (see Fig. 21). Electron microscopy,* ×52 000

fully developed muscular coats in its large vessels, additional factors to simple contractility would need to be invoked.

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References

Ashton, N. (1961). Neovascularization in ocular disease. *Transactions of the Ophthalmological Societies of the United Kingdom*, **81**, 145–161.

Ashton, N., and Tripathi, R. C. (1977). The problem of selective pericyte injury. *9th European Conference on Microcirculation, Antwerp*, 1976. Bibliotheca Anatomica, No. 16, pp. 19–23. Karger: Basel.

Ashton, N., Tripathi, B., and Knight, G. (1972). Effect of oxygen on the developing retinal vessels of the rabbit. II. In vivo experiments. *Experimental Eye Research*, **14**, 221–232.

Ashton, N., Ward, B., and Serpell, G. (1954). Effect of oxygen on developing retinal vessels with particular reference to the problem of retrolental fibroplasia. *British Journal of Ophthalmology*, **38**, 397–432.

Becker, C. G., and Murphy, G. E. (1969). Demonstration of contractile protein in endothelium and cells of the heart valves, endocardium, intima, arteriosclerotic plaques and Aschoff bodies of rheumatic heart disease. *American Journal of Pathology*, **55**, 1–37.

Burnside, M. B. (1976). Possible roles of microtubules and actin filaments in retinal pigmented epithelium. *Experimental Eye Research*, **23**, 257–275.

Burnside, B., and Laties, A. M. (1976). Actin filaments in apical projections of the primate pigmented epithelial cell. *Investigative Ophthalmology*, **15,** 570–575.

Cecio, A. (1967). Ultrastructural features of cytofilaments within mammalian endothelial cells. *Zeitschrift für Zellforschung und mikroskopische Anatomie*, **83,** 40–48.

Feeney, A., and Mixon, R. N. (1976). An in vitro model of phagocytosis in bovine and human retinal pigment epithelium. *Experimental Eye Research*, **22,** 533–548.

Gabbiani, G., Trenchev, P., and Holborow, E. J. (1975). Increase of contractile proteins in human cancer cells. *Lancet*, **2,** 796–797.

Gipson, I. K., and Anderson, R. A. (1977). Actin filaments in normal and migrating corneal epithelial cells. *Investigative Ophthalmology*, **16,** 161–166.

Goldman, R. (1975). The use of heavy meromyosin binding as an ultrastructural cytochemical method for localising and determining the possible function of actin microfilaments in non-muscle cells. *Journal of Histochemistry and Cytochemistry*, **23.** 529–542.

Grierson, I., and Lee, W. R. (1975). Pressure-induced changes in the ultrastructure of the endothelium lining Schlemm's canal. *American Journal of Ophthalmology*, **80,** 863–884.

Hogan, M. J., Alvarado, J. R., and Weddell, J. (1971). *Histology of the Human Eye*, pp. 33–35. Saunders: Philadelphia.

Holborow, E. J., Trenchev, P. S., Dorling, J., and Webb, J. (1975). Demonstration of smooth muscle contractile protein antigens in liver and epithelial cells. *Annals of the New York Academy of Sciences*, **254,** 489–504.

Kurki, P., Linder, E., Virtanen, I., and Stenman, S. (1977). Human smooth muscle autoantibodies reacting with intermediate (100Å) filaments. *Nature*, **268,** 240–241.

Kuwabara, T. (1965). Microtubules in the retina. In *The Structure of the Eye*, pp. 69–84. Edited by J. R. Rohen, Schattauer-Verlag: Stuttgart.

Kuwabara, T. (1968). Microtubules in the lens. *Archives of Ophthalmology*, **79,** 189–195.

Lazarides, E. (1975). Immunofluorescence studies on the structure of actin filament in tissues. *Journal of Histochemistry and Cytochemistry*, **23,** 507–528.

Lonchampt, M. O., Laurent, M., Courtois, Y., Trenchev, P., and Hughes, R. C. (1976). Microtubules and microfilaments of bovine lens epithelial cells: Electron microscopy and immunofluorescence staining with specific antibodies. *Experimental Eye Research*, **23,** 505–518.

Majno, G., Shea, S. M., and Leventhal, M. (1969). Endothelial contraction induced by histamine-type mediators: an electron microscopic study. *Journal of Cell Biology*, **42,** 647–672.

Piatigorsky, J., Webster, H., and Wollberg, H. (1972). Cell elongation in cultured embryonic chick lens epithelium with or without protein synthesis. *Journal of Cell Biology*, **55,** 82–92.

Pollack, R., Osborn, M., and Weber, H. (1975). Patterns of organisation of actin and myosin in normal and transformed culture cells. *Proceedings of the National Academy of Sciences of the United States of America*, **72,** 994–998.

Pollack, R., and Rifkin, D. (1975). Actin-containing cable within anchorage-dependent rat embryo cells are dissociated by plasmin and trypsin. *Cell*, **6,** 495–506.

Pollard, T. D., and Weihing, R. R. (1974). Actin and myosin and cell movements. *Critical Reviews in Biochemistry*, **2,** 1–65.

Rafferty, N. S., and Esson, E. A. (1974). An electron-microscope study of adult mouse lens: some ultrastructural specializations. *Journal of Ultrastructural Research*, **46,** 239–253.

Rahi, A. H. S., Holborow, E. J., Perkins, E. S., Gungen, Y. Y., and Dinning, W. J. (1976). Immunological investigations in uveitis. *Transactions of the Ophthalmological Societies of the United Kingdom*, **96,** 113–122.

Rathke, D., Schmid, E., and Franke, W. (1975). The action of the cytochalasins at the subcellular level. *Cytobiologia*, **10,** 366.

Rhodin, J. A. G. (1967). The ultrastructure of mammalian arterioles and precapillary sphincters. *Journal of Ultrastructural Research*, **18,** 181–223.

Trenchev, P., Dorling, J., Webb, J., and Holborow, E. J. (1976). Localisation of smooth muscle-like contractile proteins in kidney by immunoelectron microscopy. *Journal of Anatomy*, **121,** 85–95.

Trenchev, P., and Holborow, E. J. (1976). The specificity of antiactin serum. *Immunology*, **31,** 509–517.

Trenchev, P., Sneyd, P., and Holborow, E. J. (1974). Immunofluorescent tracing of smooth muscle contractile protein antigens in tissues other than smooth muscle. *Clinical and Experimental Immunology*, **16,** 125–136.

Tripathi, B., Ashton, N., and Knight, G. (1973). Effect of oxygen on the developing retinal vessels of the rabbit. III. Mode of growth of rabbit retinal vessels in tissue culture. *Experimental Eye Research*, **15,** 321–351.

Tripathi, B., Knight, G., and Ashton, N. (1974). Effect of oxygen on the developing retinal vessels of the rabbit. IV. Effect of hyperoxia on rabbit retinal vessels in tissue culture. *Experimental Eye Research*, **19,** 449–475.

Wessells, N. K., Spooner, B. S., Ash, J. F., Bradley, M. O., Luduena, M. A., Taylor, E. L., Wrenn, J. T., and Yamada, K. M. (1971). Microfilaments in cellular and developmental processes. *Science*, **171,** 135–143.

Wiedeman, M. P. (1963). Circulation. In *Handbook of Physiology*, Section 2. Edited by W. F. Hamilton and P. Dow. American Physiological Society: Washington.

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Television slit-lamp biomicroscopy

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SUMMARY The basic requirements for performing television slit-lamp biomicroscopy are outlined, and the methods of demonstrating particular features of ocular anatomy and ocular disease are discussed. The technique has a particular role in teaching in the clinical setting.

Television has been used for many years to document and display ophthalmic procedures and clinical disorders. The modular construction of the Zeiss series of biomicroscopes makes it possible to carry out successful video-photography with the slit-lamp, using the same attachments employed for televising ocular surgery. This creates a most valuable teaching tool with some potential for research use. The following paper details the requirements for successful television slit-lamp biomicroscopy.

Materials and methods

Slit-lamp
A standard Zeiss slit-lamp may be used (Fig. 1) but the results may be affected by differing combinations of accessory equipment.

Video equipment
The basic requirement for simple display work (surveillance) is a television camera and monitor. To record observations a videotape recorder (or VTR) is required. It is not the purpose of this paper to discuss the relative merits of different commercial equipment, since the final choice will depend on factors of cost or the adaptation of existing equipment. The present report rests on experience gained with the Sony camera AUC 3420CE and portable VTR (AU 3420CE) (i.e., the Sony 'Rover' system) and Pye 11 inch (28 cm) precision monitor (842843/01) for black-and-white. For colour a Shibaden camera (HV 1500) × (HV9015) was used with a Hitachi 18 inch (45 cm) colour monitor (CM 181U). The Hitachi colour VCR with the Pal-Secam cartridge system was used (SV 630). Also in the United States the Circon Camera and Sony Trinitron monitor have proved satisfactory. The slit-lamp and video requirements are summarised in Table 1.

TECHNICAL POINTS

Field of view
For general surveillance of the eye in diffuse white light it is important to be able to display the whole of the palpebral aperture without 'scanning' with

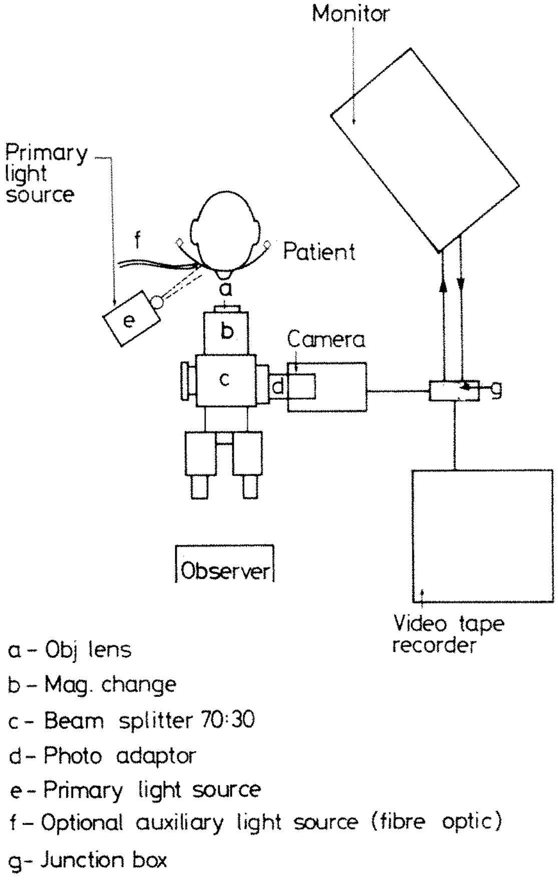

Fig. 1 *The arrangement of the television slit-lamp biomicroscopy*

Address for reprints: Mr A. J. Bron, FRCS, The Eye Hospital, Walton Street, Oxford OX2 6AN the slit lamp. This requires that the field of view in the horizontal meridian at the lowest magnification of the slit lamp is at least 3·0 cm. This is also important when examining the tear film using fluorescein in the conjunctival sac, since an excellent opportunity is afforded to watch both the marginal strip of tears and precorneal tear film simultaneously.

The fields of view for varying combinations of the slit lamp, magnification change, and photo-adaptor combinations are given in Table 2.

LIGHT SOURCES

The primary light source (slit source) may be used for surveillance of the eye in diffuse illumination (white light) or for fluorescein work (blue light).

Table 1 *Slit-lamp requirements for television biomicroscopy*

1. Zeiss slit lamp (100/16)
   or photo slit lamp
2. Objective lens
   100 mm
   125 mm Photoslit
3. Single beam splitter (70:30)
4. Photo-adapter
   137 mm
   107 mm
5. Magnification change
   Manual
   Zoom
6. Illumination sources
   (a) Slit source (primary illuminant). Overload facility of value
   (b) Additional source (secondary illuminant)
7. Microscope height adjustment
   (a) Joystick (manual)
   (b) Column (manual)
   (c) Motorised
8. Video equipment
   (a) Camera
   (b) Monitor
   (c) VTR

Table 2

Slit lamp		*Photo-adapter number*	*Smallest horizontal diameter (mm)*	*Smallest diagonal diameter (mm)*	*Smallest vertical diameter (mm)*
Regular	Manual	137	15	19	11
		107	20	25	15
	Zoom	137	12	15	9
		107	16	20	12
Photoslit	Manual	137	20	23	15
		107	25	29	18
	Zoom	137	16	18	14
		107	13	16	10

Diffuse illumination

The pool of light can be enlarged to cover the whole of the palpebral aperture by placing a standard diffusing filter over the slit source. Alternatively less costly diffusers are easily produced from paper or opalescent plastic sheets cut to size.

Fluorescein work

Exciter filter

It is important to use an interference filter (e.g., Baird Atomic No. 5 Spectrotech SE 40 or Balzar FITC 4) to produce the blue exciter source, since even with such a source the intensity of illumination may be less than optimal. With a blue exciter filter over the 1° source, opened wide, the pool of blue light does not encompass the whole palpebral aperture. It would be useful to enlarge the pool of light, but this problem has not yet been solved with existing equipment. Two solutions have been considered. (*a*) The pool of light can be enlarged by placing a diverging lens over the 1° light source in addition to the blue filter. However, this so reduces the intensity of illumination that the technique appears to have little application. (*b*) An alternative technique, which will probably be adopted ultimately, is to place the blue exciter filter over a secondary (e.g., fibreoptic) light source with delivery of the light close to the eye.

Barrier filter

A barrier filter, such as a gelatin absorption filter (e.g., Ilford 110) placed over the objective lens of the slit-lamp is essential for examination of the marginal strip of tears, the preglobar and precorneal tear films, and for negative and positive staining of the cornea (e.g., dry spots and ulcers). A matched interference filter is the ideal to provide maximum illumination, but a suitable absorption filter will do.

A barrier filter is both unnecessary and undesirable for the demonstration of the rings of applanation during applanation tonometry. Use of the barrier filter reduces illumination to unsatisfactory levels, and the rings are clearly visible without it.

Secondary light source

A bright secondary illuminant is required, particularly to provide background illumination during slit microscopy. Unfortunately the secondary source of the photoslit lamp is not intense enough. However, it is easy to supply another lamp for this purpose, and a fibreoptic source controlled by a rheostat and located close to the objective lens of the slit lamp proves to be satisfactory.

Televising the slit image

Placing the slit image on the screen is at first disap-

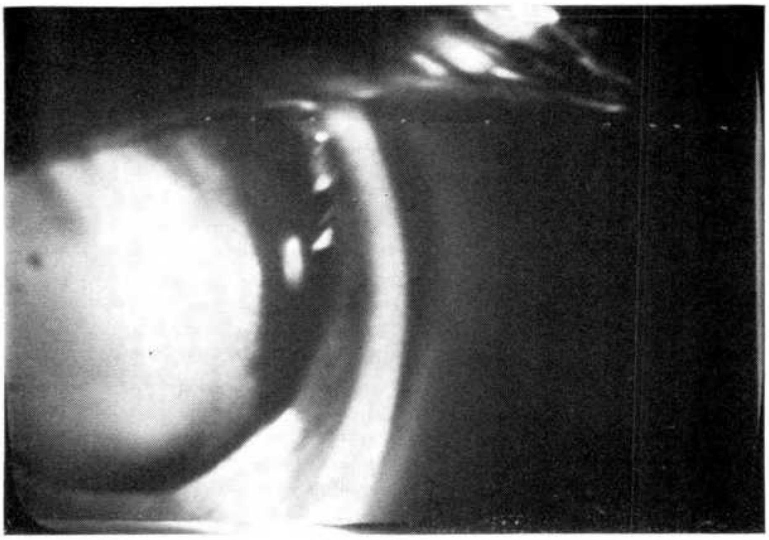

Fig. 2 *Slit picture of the anterior segment*

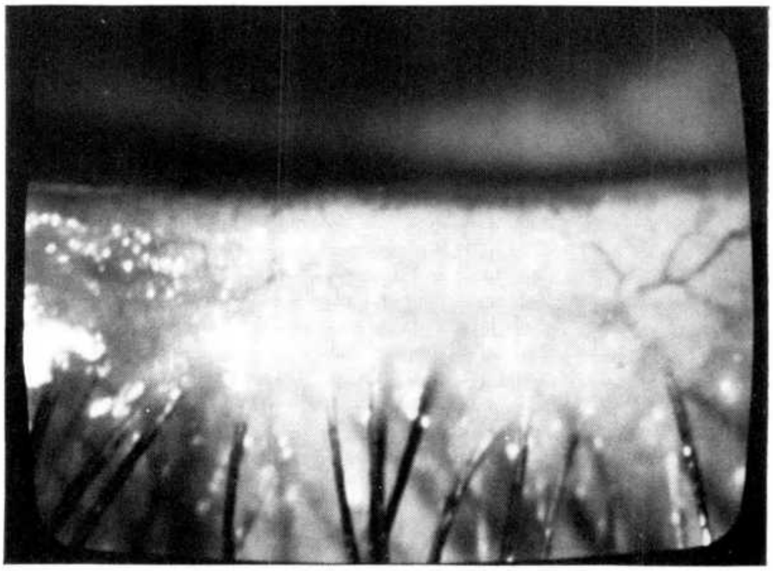

Fig. 3 *Lower lid margin seen by broad focal illumination*

pointing because of the great contrast between the light on the object of interest, e.g., cornea or lens, and the surrounding structures, which are not illuminated directly. This problem is readily negotiated by adding a secondary fibreoptic source (see above) to provide background illumination. This technique is identical to that required for slit photography using a photoslit-lamp camera (Fig. 2).

Scleral scatter illumination

With the pupil dilated scleral scatter illumination will demonstrate epithelial corneal oedema. The available intensity from the primary light source is not adequate to do this well, however.

MANOEUVRING THE MICROSCOPE

When recording sequences for clinical documentation it is important to achieve smooth transitions from one mode of examination to another. The observer must retain focus when shifting the microscope to different points of interest in the eye or when changing magnification. The following points may be made:

Horizontal traverse of the microscope is achieved easily and smoothly with the joystick control.

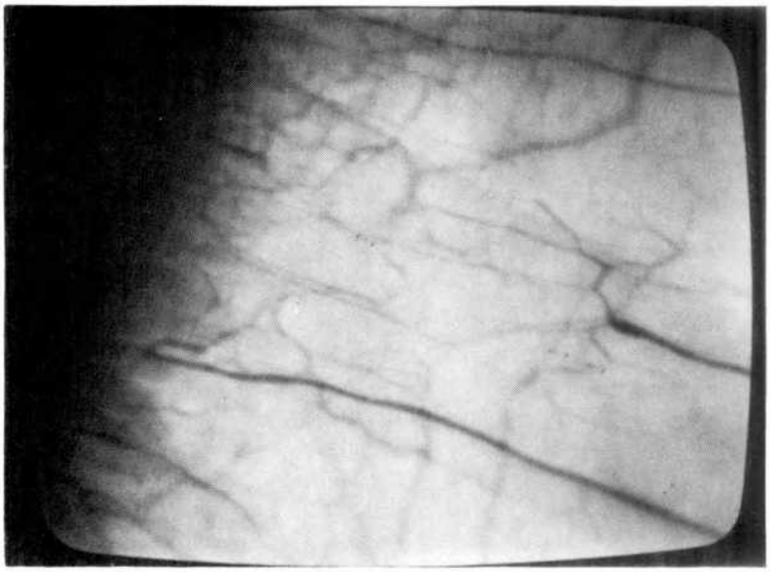

Fig. 4 *Perilimbal bulbar conjunctival vessels (diffuse illumination)*

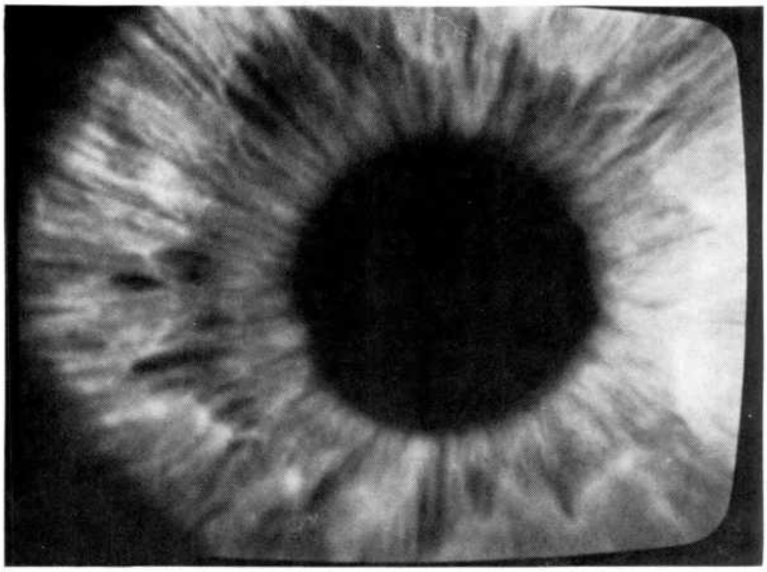

Fig. 5 *The iris collarette seen by diffuse illumination*

Vertical movement may be achieved adequately by manual controls such as the knurled ring on the central column or, better, rotation of the joystick control. Motorised controls with the switch are within easy reach of the hand holding the joystick. The weight of the camera becomes a critical consideration during the 'up' movement and may on occasion demand manual assistance.

The click-stop manual magnification change is satisfactory, but not ideal, since a series of dark periods occur on the screen at each change, which interrupts the continuity of observation. The foot-operated motorised zoom is ideal for television slit-lamp biomicroscopy because it allows the user to convert a survey picture into a detailed scrutiny at high magnification. Both the motorised zoom and vertical movements permit smooth titling using typescript. This can reduce editing problems at a later date.

APPLICATIONS OF TELEVISION BIOMICROSCOPY

The majority of anterior segment features studied with the slit-lamp are amenable to scrutiny by slit-lamp television biomicroscopy.

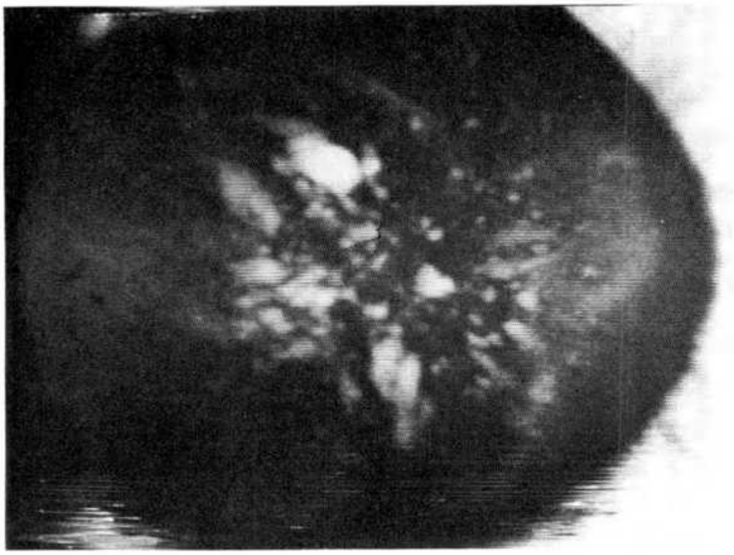

Fig. 6 *Cortical lens opacities seen in the dilated pupil (photographs taken from 'stop frame' are of lower quality)*

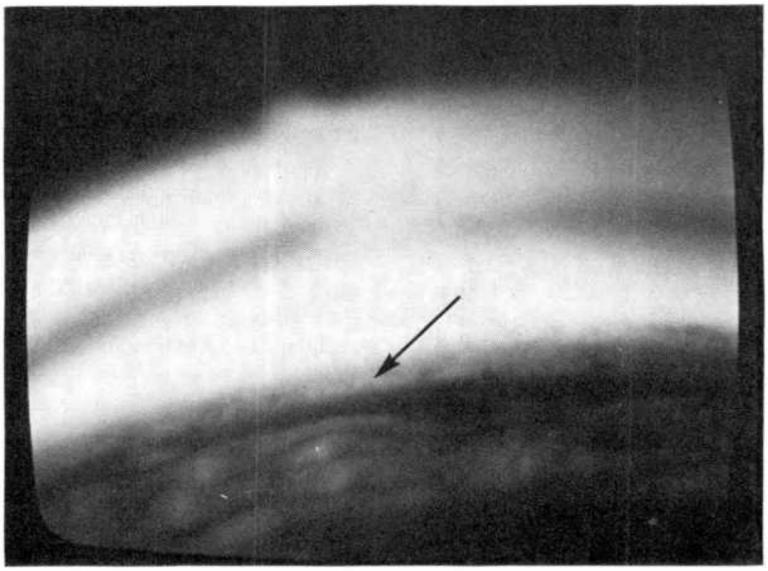

Fig. 7 *Gonioscopy: a lightly pigmented open angle, with visible iris processes*

The lids
The lid margins, including lacrimal puncta and Meibomian orifices, may be demonstrated at high magnification with diffuse or focal illumination (Fig. 3). Expression of Meibomian oil may be shown by catching the specular reflex from the oil dome. The palpebral conjunctival vessels may be shown with diffuse illumination, or at high magnification, with red-free light.

The Globe
The globe vessels are well demonstrated in diffuse light, and at high magnification red-cell flow may be demonstrated. To show the limbal vessels, i.e., the marginal corneal arcade, retroillumination using the slit source is satisfactory, and a background illuminant should also be used. The contour of the globe can be examined in specular light from the tear film (Fig. 4).

The tear film
With high magnification and reduced intensity of illumination the typical coloured interference pattern produced by the surface Meibomian oil may

Table 3 *Video techniques*

Technique	*Purpose*	*Primary source*	*Secondary source*	*Filter*	*Magnification*	*Notes*
Survey (diffuse illumination)	General detail	+	–	Diffuser	Any	Low mag. to show whole of palpebral aperture. High mag. for conjunctiva, globe, vessels, Meibomian orifices and specular reflex of tear film
Fine slit (focal)	Thickness of objects in section. Also location of depth of objects in section	+	+ Added fibre-optic or other source	–	Any	(1) Show thickness and shape of cornea (2) Depth of chamber (3) Opacities in cornea and lens (4) Flare and cells in anterior chamber?
Broad slit (focal)	Used with slit angled obliquely to illuminate objects which scatter light	+	+	–		For punctate epithelial keratitis opaque microcysts
Retroillumination (against iris)	Shows objects in silhouette; refractile objects	(Fine or broad slit)	+ (May not be needed for HP)	–	Any	Limbal vessels, e.g., pannus, corneal lesions, e.g., clear microcysts, superficial corneal disorder (SCD)
Retroillumination (against red reflex: slit offset to one side or other to avoid corneal reflex)	As above	+ (Broad slit)	–	–	Any	Ideal to show fine detail of structures in cornea or lens, differing from surrounding structures in refractive index, e.g., microcysts and SCD
Specular reflection	To examine: (*a*) specular reflex of tear film, e.g., interference pattern (*b*) Endothelial specular zone (*c*) Internal specular reflection	+	–	–	Any	Endothelial mosaic is visible at high magnification
Scleral scatter (broad strip at either limbus)	To show light-scattering structures in the cornea, e.g., epithelial oedema	+	–		LP–HP	Best at low power with TV because of low emittence level
Dyes: Fluorescein	(*a*) Negative staining follicles; fingerprint lines	+ Large pool	?+	Blue exciter yellow barrier	LP–HP	HP poor at low light levels
	(*b*) Positive staining punctate epithelial erosion, ulcer	+ Large pool of light	?+	Blue exciter yellow barrier		
	(*c*) Applanation	+	–	Blue filter only		

HP = high power. LP = low power

be seen or accentuated by narrowing the palpebral aperture, using specular examination. The marginal strip and tear film debris are also demonstrated.

With the use of fluorescein and the appropriate exciter and barrier filters (see above) the marginal strip, prebulbar, and precorneal tear films are graphically demonstrated, as is the replenishment of the tear film which accompanies each blink. Negative and positive staining can also be shown.

The cornea

Numerous features of corneal disease may be demonstrated by slit, focal, and retroillumination. The fine detail of vesicular epithelial oedema, finger-print lines, and bleb-like dystrophies are well seen by retroillumination against the iris or red reflex. Scars may be shown in slit section and diffuse or focal illumination, while density may be suggested by retroillumination. The latter technique has also proved ideal for demonstrating corneal vessels and splits in Descemet's membrane in buphthalmos. Scleral scatter will demonstrate epithelial oedema against the dilated pupil. Specular examination is just capable of resolving the cells of the endothelium, but the tear film highlight diminishes the value of using this technique except to demonstrate how it is done. It should be possible in future to limit the occurrence of such 'hot spots' on the screen electronically.

The iris

The architecture of the iris and the mobility of the pupil are shown well by diffuse illumination (Fig. 5).

The lens

With the pupil dilated the detail of a clear lens, including the anterior clear zone, may be shown in slit section. Certain lens opacities may be shown in focal illumination (Fig. 6) while others are best seen against the red reflex. Still other opacities may be demonstrated as contour changes within the cortex by means of the specular technique.

The vitreous
The normal vitreous architecture is difficult to display, but significant opacities may be shown in focal and retroillumination.

The fundus
With a fundus contact lens in place the disc and its vessels can be shown. Venous pulsation at the disc may be a striking phenomenon. Demonstration of macula and vessels, lesions such as new vessels, and haemorrhage has been achieved but has not been fully satisfactory. Colour is essential here, since colour contrasts are important.

Gonioscopy
The angle structures are well seen, so that television has particular teaching value in this area (Fig. 7).

Some of the greatest problems encountered occur when illumination is moved from a highly reflecting surface such as the sclera to a poorly reflecting surface such as the iris. This may be most marked, for instance, with a dark brown iris. The problem may be overcome at times by using secondary illumination, but at others it may have to be accepted that in a given patient it may not be possible to display adequately a given mode of examination on the television screen.

Discussion

The technique of television biomicroscopy has its greatest use in the teaching of medical students. The teaching of ophthalmology is often condensed and makes severe demands on the keenest of teaching staff. One of the greatest problems relates to the difficulty of making observations accessible to the student. By using the television slit lamp the teacher cuts down a great deal of the repetition when students are obliged one by one to look down an observer tube. Instead he can point out features which appear on the screen and indeed may make adjustments to the slit lamp while observing the screen himself.

Observations which are usually not easy to demonstrate, such as the applanation rings or the chamber angle, can be discussed with the student group looking at the phenomenon at the same time. The dynamic components of the features examined, such as blinking, blood flow, pupil constriction, pulsation of the applanation rings, and the venous pulse at the disc, all add to the interest generated by the technique. It is clear that the resolution of most television systems is sufficient to demonstrate all the clinical problems normally studied with the biomicroscope. There is, however, room for improvement, and it is likely that selection of low-weight, high-resolution cameras, of low-light-level cameras, the use of image intensifiers, and improved illumination sources will bring about these improvements. A streamlined custom-built television slit lamp, embodying some of the ideal features mentioned above, would also be a welcome addition to the clinical armamentarium.

Other uses and improvement may be foreseen for the future. The use of a 'special effects generator' would allow the combination of clinical observations with temporally related information on the same screen. An example would be to combine the applanation rings with the pressure reading dial during tonometry, or of disc vessel pulsation during ophthalmodynamometry, with a simultaneous reading of force applied to the globe. It must be anticipated that fluorescein angiography of the anterior segment will be feasible by this technique, and that the time after injection could similarly be displayed on the screen.

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B-scan ultrasonography of the anterior segment of the eye

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SUMMARY B-scan ultrasonograms of the anterior segment were performed on selected patients. The difficulties in imaging the anterior segment are discussed and the value of this technique is demonstrated by illustration of B-scans in different pathological conditions. This technique can often provide important information and allow an early and accurate prognosis.

B-scan ultrasonography is now widely used in ophthalmology for investigation of orbital lesions and posterior segment lesions when direct visualisation is prevented by opacity in the ocular media. Most authors have concentrated on ultrasonic demonstration of posterior segment lesions, but the separation of diseases of anterior and posterior segments is largely artificial. The present study has perpetuated this division, but in an attempt to demonstrate the diagnostic value of ultrasound in involvement of the anterior segment.

The normal practice of this laboratory has been to include the cornea, iris, and lens on ultrasonograms to aid orientation of B-scan pictures by clinicians. This has led to an increasing demand for information on anterior segment lesions alone.

The difficulties of ultrasonic visualisation of the anterior segment will be considered. The demand for anterior segment ultrasound led to an appraisal of the problems, and the experience gained in the examination of the first 500 patients has led to the development of a satisfactory routine. Cases are presented to illustrate the use of conventional ultrasonic equipment in the management of patients with anterior segment disease.

Materials and methods

Approximately 500 patients have been examined in the first 2 years of a recently established diagnostic ultrasonography clinic, and of these 7 patients will be used to illustrate the most common diagnostic problems. The clinic is one in which both ophthalmologists and radiologists experienced in ultrasonic imaging techniques participate.

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Ultrasonic examination is with the Sonometrics 100 Ophthalmoscan (Coleman *et al.*, 1969), a purpose-built scanner assembled for high resolution ophthalmic application. It is possible to image the anterior segment with this equipment. The acoustic coupling is by the waterbath technique previously described by Coleman *et al.* (1969). The contact B-scanner (Bronson and Turner, 1973) does not image the anterior segment unless a waterbath is used.

After light topical anaesthesia a Barraquer type wire speculum is inserted to keep the eye open. It has been found that resolution is improved if the transmitted and reflected impulses do not pass through the closed eyelids. Probes of nominal frequencies of 15 and 20 MHz are used for the study of the anterior segment and the highest available magnification of × 5 is used. Comparable values for posterior segment work would be 8 or 10 MHz at a magnification of × 3. The scans are photographed from an oscilloscope display to produce Polaroid prints. Total examination time is less than 30 minutes.

NORMAL ULTRASONIC ANATOMY

An ultrasonogram of a normal anterior segment produced in the manner described is shown in Fig. 1. This defines the anterior and posterior corneal surfaces, and small echoes are seen within the corneal stroma. The depth of the anterior chamber and the configuration of the iris are clearly seen, and both corneal thickness and anterior chamber depth are demonstrated. These measurements can be made with a high degree of accuracy by the facility of simultaneous A- and B-scan display provided by the Sonometrics 100 apparatus. The anterior lens surface is not shown in this view in which the pupil has been demonstrated. The interior of the lens is echo free.

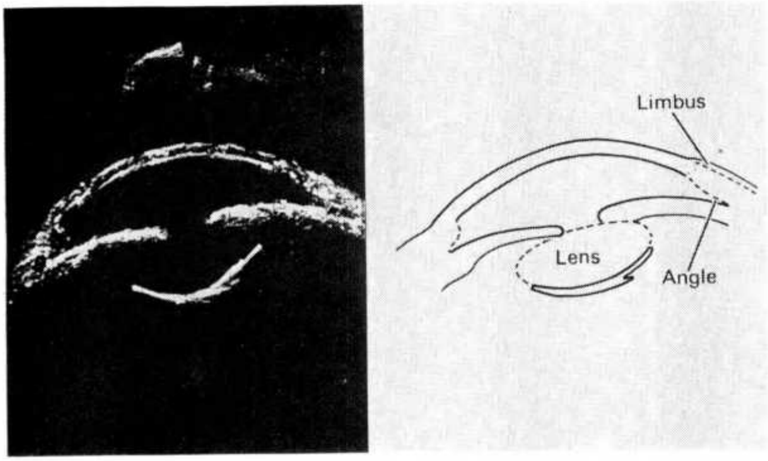

Fig. 1 *B-scan ultrasonogram of normal anterior segment*

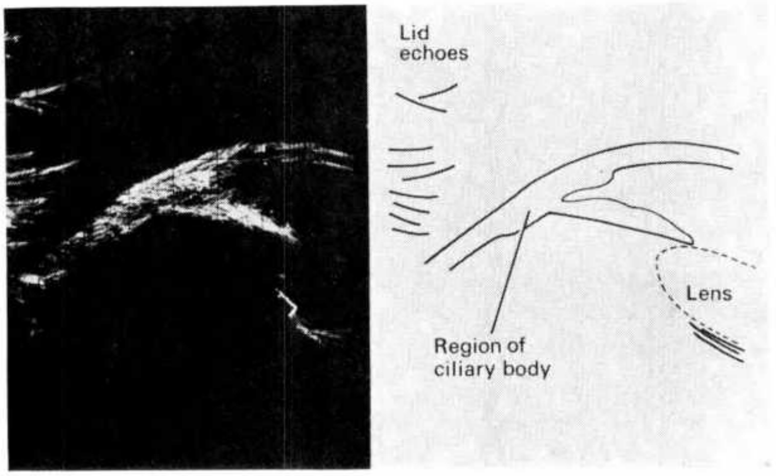

Fig. 2 *Normal eye to show lateral side of anterior segment*

The region of the ciliary body can also be explored (Fig. 2) and ciliary processes are occasionally identified. Tumour masses can be visualised and their extent defined before local excision.

CASE REPORTS

A. *Corneal opacity*

Case 1. A 57-year-old man presented with a 10-year history of recurrent episodes of discomfort in his left eye. The vision had been poor since an injury in 1948, and at the time of examination the vision in the left eye was hand movements. An opaque cornea prevented further clinical examination. Ultrasonic examination showed an anatomically normal lens and iris and a cornea with a relatively normal periphery. A 7-mm penetrating keratoplasty was undertaken, and the patient attained a corrected acuity of 6/9 after an uneventful postoperative course. Pathological examination showed keratinoid corneal degeneration (Garner, 1970) in the excised disc. The abnormal area appears in the ultrasonogram as a dense, echo-rich area in the anterior stroma.

Case 2. A 47-year-old woman with postherpetic scarring of the cornea was examined. Two previous penetrating grafts and a lens extraction had been performed. The ultrasonogram showed an aphakic eye with a thin iris. The most normal echo pattern was in the centre. The cornea was otherwise extensively thickened. In view of the predicted technical difficulties of grafting into a greatly thickened cornea further surgery was postponed.

Case 3. A 13-year-old boy with postherpetic corneal scarring developed secondary bacterial infection and ulceration of the central cornea. He presented with central corneal perforation, and an emergency penetrating keratoplasty was performed.

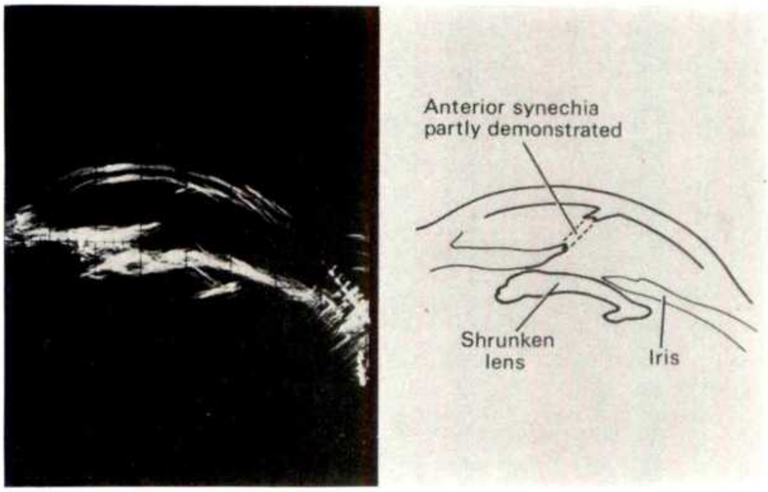

Fig. 3 *Longstanding traumatic cataract from central corneal penetrating wound (Case 4)*

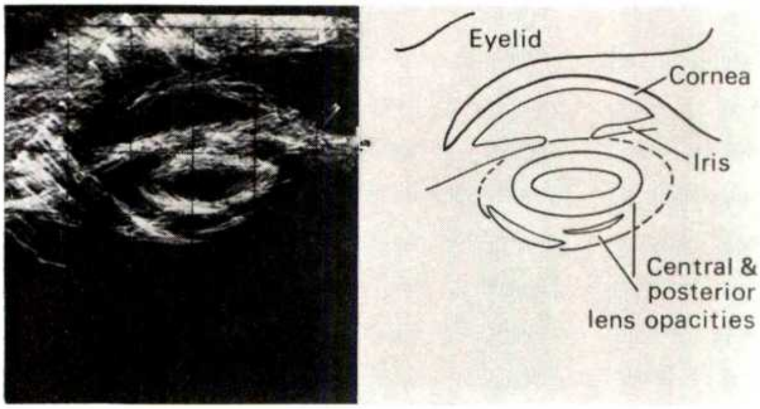

Fig. 4 *Ultrasonic appearance of senile cataract*

Postoperatively the anterior chamber was slow to form owing to leakage of aqueous at the suture line, and vascularisation of the wound from the iris occurred. There was retrograft membrane formation, and the graft became opaque obscuring the anterior chamber. Ultrasonic examination showed a thickened donor graft with a shallow anterior chamber, and adhesions between iris and suture line were demonstrated. More recently a further graft has been performed. With the information available from the ultrasound examination care was taken during surgery to trephine into the formed part of the anterior chamber, avoiding the lens. The recent graft has been successful and reasonable vision has been achieved.

B. *Opacities in the lens*

Case 4. A patient aged 23 had a totally opaque lens following a penetrating corneal wound in childhood. A narrow strand of iris was adherent to the corneal scar. The patient was referred for ultrasound to exclude posterior segment abnormality before extracapsular extraction. The anterior segment views (Fig. 3) showed a shrunken lens with almost total absorption of lens matter. It was suggested that capsulotomy would be the more appropriate operation, but surgery has not yet been performed. The appearance of a senile cataract is shown in Fig. 4 for comparison.

C. *The traumatically disorganised eye*

Case 5. A young man was examined after a blunt injury to 1 eye. A total hyphaema prevented any detailed examination of the injured eye. Ultrasound in the acute phase (Fig. 5) showed subluxation of the lens and an artificially deep anterior chamber, suggesting the likelihood of angle recession. The patient was given a poor prognosis immediately after injury, when the only apparent defect was a total hyphaema.

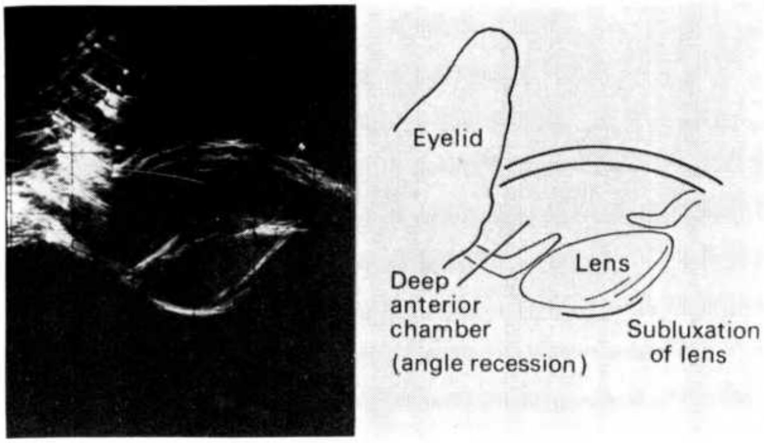

Fig. 5 *Case of total hyphaema. Demonstration of subluxation of the lens (Case 5)*

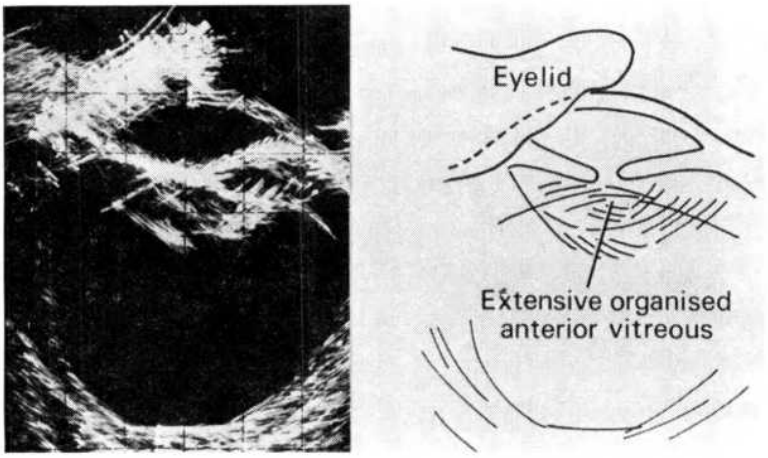

Fig. 6 *Extensive anterior vitreous organisation following trauma (Case 6)*

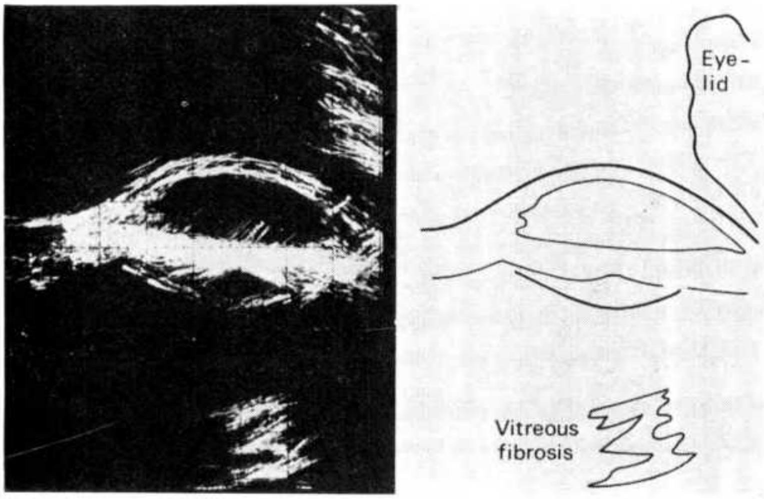

Fig. 7 *Showing separate nature of fibrosis in the vitreous unlikely to complicate lens extraction (Case 7)*

Case 6. Figure 6 shows the eye of a 4-year-old boy after traumatic corneal perforation by a stone. The clinical appearance at this stage was of traumatic cataract; a folded anterior lens capsule was visible through a miosed and adherent pupil. Ultrasonography during general anaesthesia showed extensive involvement of anterior vitreous and lens in what is presumed to be fibrotic process following rupture of the lens capsule. Anterior vitrectomy was considered but was not carried out at this time. A different decision would probably now be made with the availability of a suction/infusion cutter. The patient retains his eye, although useful vision is absent.

Case 7. A situation essentially similar to that in the previous patient is seen in Fig. 7. This patient also has a small and adherent pupil and an opaque lens, but vitreous fibrosis is separate from lens and is unlikely to complicate successful surgery.

Discussion

Ultrasonography is a useful method of visualising the structure of a diseased or opaque eye. Conventional ultrasonograms often include imaging of the anterior segment as part of the completed picture, and early illustrations by Baum and Greenwood (1958, 1960, 1961) include some easily recognisable anterior segments. Coleman and colleagues (Coleman *et al.*, 1969; Coleman, 1972; Coleman *et al.*, 1973a, b) have improved ultrasonic apparatus and techniques and have illustrated a normal anterior segment in early papers. Coleman *et al.* (1969) and Vanysek *et al.* (1969) reported a series of 25 normal and aphakic eyes in which imaging of the anterior segment was attempted.

The reasons for the paucity of reports of anterior segment appearances are worth consideration. Disease of the anterior segment is frequently visible by conventional examination, and further information is often not required. The current case reports have attempted to show examples from patients in whom ultrasound has contributed further useful information. For example, more extensive pathology can be concealed by an opaque cornea or hyphaema (Coleman, 1973a, b). Ultrasonography is probably essential prior to vitrectomy (Coleman, 1972; Jack *et al.*, 1974), and even negative results are reassuring when surgery is being contemplated.

Ultrasonic visualisation of the anterior segment can be technically difficult. Some apparatus is designed to be in contact with the eyelid, and echoes from the cornea are indistinguishable from those of the posterior surface of the eyelids. There would also appear to be considerable absorption and scattering of sound waves during transmission through the eyelids, particularly with the higher frequencies used in ophthalmology, and this contributes further to poor imaging.

Ultrasonic probes may give poor resolution of detail in the anterior segment. Probes are designed to give maximum lateral resolution near the focal length, which is often designed to coincide with the posterior coats of the eye, and anterior segment detail is again poor. The probe is engineered to both transmit and receive the ultrasonic impulses and if situated close to the cornea is still refractory or 'ringing' from the transmitted pulse when the first reflected waves are received. Echoes from parts of the anterior segment therefore fail to show.

These problems have been overcome to a large extent by improved design of probes. It is possible to narrow the beam width by focusing sound in much the same fashion as light is focused, and to reduce 'ringing' by damping the crystal with a backing usually consisting of epoxy resin and powdered tungsten. Excessive damping of the crystal may further reduce the sensitivity of the device, and so a 'near field' is usually left in which imaging is not satisfactory. The anterior surface of the lens is usually difficult to image owing partly to dispersal of the sound beam by the convex anterior surface and partial concealment by the iris. With a dilated pupil the lens is easily imaged (Posakony, 1969; Gordon, 1969).

Many of these problems are overcome if the waterbath technique is used (Coleman *et al.*, 1969) and the eye is kept open during the examination. In practice the distance of the probe from the cornea is usually 10 to 20 mm, and the problem of the focal length being posterior to the eye does not appear to be of great importance.

Using a frequency higher than 10 MHz improves resolution, perhaps because less damping is required in a high frequency probe (Posakony, 1969) rather than an improvement due to frequency alone. The use of purpose-designed ophthalmic ultrasound apparatus is recommended. The magnification which can be obtained improves resolution rather than merely increasing the size of the image. As recently as 1971 Sokollu (1971) thought equipment design to be the main cause of poor imaging of the anterior segment. Most problems seem to have been overcome in the Sonometric apparatus.

Finally the patient's eyes must be immobile during the few seconds necessary for the recording of each scan to improve resolution further. This can be assured only with a relaxed patient, and the confidence and skill of the operator contribute much to the patient's mental state.

The indications for ultrasonography have been listed by Coleman *et al.* (1973b), and their criteria may be applied to patients with anterior segment disease as follows: (1) Opaque cornea; (2) opaque anterior chamber (hyphaema, etc); (3) opaque lens, but not *senile* cataract if other tests of function are normal; (4) small pupil ± opaque lens; (5) anterior vitreous pathology; (6) tumours of the iris or ciliary body.

Ultrasound is generally used to complement existing techniques of examination. In the opaque eye for example a combination of ultrasonography and electrophysiology is valuable (Kennerdell, 1973). The improving quality of ophthalmic B-scans using conventional purpose-designed equipment can give valuable information in deciding the management of selected patients.

Thanks are due to Professor W. S. Foulds and consultant ophthalmologists of the Ophthalmic Division who referred patients. Dr P. Morley and Dr E. Barnett, of the Departments of Radiology and Ultrasonography, offered much helpful advice. I am grateful to Dr W. R. Lee, ophthalmic pathologist, for access to his files and for his advice.

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References

Baum, G., and Greenwood, I. (1958). The application of ultrasonic locating techniques to ophthalmology—II. Ultrasonic slit lamp in the ultrasonic visualisation of soft tissues. *Archives of Ophthalmology*, **60**, 263–279.

Baum, G., and Greenwood, I. (1960). Ultrasound in Ophthalmology. *American Journal of Ophthalmology*, **49**, 249–261.

Baum, G., and Greenwood, I. (1961). A critique of time—amplitude ultrasonography. *Archives of Ophthalmology*, **65**, 353–365.

Bronson, N. R., and Turner, F. T. (1973). A simple B-scan ultrasonoscope. *Archives of Ophthalmology*, **90**, 237–238.

Coleman, D. J., Konig, W. F., and Katz, L. (1969). A hand-operated ultrasound scan system for ophthalmic evaluation. *American Journal of Ophthalmology*, **68**, 256–263.

Coleman, D. J. (1972). Ultrasound in vitreous surgery. *Transactions of the American Academy of Ophthalmology and Otolaryngology*, **76**, 467–477.

Coleman, D. J., Jack, R. L., and Franzen, L. (1973a). Ultrasonography in ocular trauma. *American Journal of Ophthalmology*, **75**, 279–288.

Coleman, D. J., Jack, R. L., and Franzen, L. (1973b). Ultrasonography in Pediatric Ophthalmology. *Journal of Pediatric Ophthalmology*, **9** (2), 111–119.

Garner, A. (1970). Keratinoid corneal degeneration. *British Journal of Ophthalmology*, **54**, 769–780.

Gordon, D. (1969). Transducer Design for ultrasonic ophthalmology. In *Ophthalmic Ultrasound*, pp. 65–68. Edited by K. A. Gitter. Mosby: St. Louis.

Jack, R. L., Hutton, W. L., and Machemer, R. (1974). Ultrasonography and vitrectomy. *American Journal of Ophthalmology*, **78**, 265–274.

Kennerdell, J. S. (1973). Evaluation of eyes with opaque anterior segments, using both ultrasonography and electroretinography. *American Journal of Ophthalmology*, **75**, 853–860.

Posakony, G. J. (1969). Ultrasonic transducers and acoustic waves. In *Ophthalmic Ultrasound*, pp. 7–17. Edited by K. A. Gitter. Mosby: St. Louis.

Sokollu, A. (1971). The present stage and future trends of ultrasonic techniques in eye diagnosis. In *Ultrasonographia Medica*, Vol. 2, pp. 127–131. Edited by J. Bock and K. Ossoinig. Wiener medizinischen Akademie: Vienna.

Vanysek, J., Preisova, J., and Paul, M. (1969). Ultrasonic image of the anterior eye segment by TAU and SIMU. In *Ophthalmic Ultrasound*, pp. 213–217. Edited by K. A. Gitter. Mosby: St. Louis.

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Cine photography and video recording of anterior segment fluorescein angiography

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SUMMARY A description is given of apparatus and technique for carrying out cine photography and video recording of anterior segment fluorescein angiography. We found cine best for single-frame analysis and video tape recording less expensive.

Anterior segment angiography was introduced 10 years ago on the fundus camera (Jensen and Lundback, 1968) and on the slit lamp camera 9 years ago (Brun-Jensen, 1969; Mitsui *et al.*, 1969). It was found to provide useful information on conjunctival and corneal lesions, especially in lipid keratopathy (Bron and Easty, 1970). Abnormal vascularity of the iris is particularly well demonstrated in anterior segment ischaemia (Chignell and Easty, 1971; Marsh *et al.*, 1974), in glaucoma (Vannas, 1969), in diabetes (Cobb, 1968; Jensen and Lundback, 1968), and after central retinal vein and artery occlusions (Raitta and Vannas, 1969; Mapstone, 1970; Kottow, 1976; Laatikainen and Blach, 1977).

One of the major photographic defects which soon becomes apparent in anterior segment angiography is that the standard machines do not give a fast enough sequence of photographs during the early phase of fluorescein filling. This is important because in diseased states of the anterior segment significant changes in the vascular pattern and permeability occur within the first 5 seconds of fluorescein appearing within the eye. In our experience with the Zeiss photo-slit lamp at best we could obtain 6 consecutive exposures at 1 second intervals, after which there was a delay of 13 seconds for recycling.

We set out therefore to develop a cine technique so that these very early stages of vascular fluorescein filling could be analysed. We decided at the same time that we should also take standard 35 mm pictures at 1·5-second intervals. The basic unit was a Carl Zeiss photo-slit lamp. The flash tube was driven by a Siemens power pack which was shared with a Zeiss fundus camera. The footpedal and motor drive were also shared. A 70/30 beam splitter was placed in the optical pathway. A standard Zeiss tube with a motorised Nikon camera back attached to it was fitted on one limb. A cone containing a Spectrotech SB5 barrier filter was mounted in the camera. The diaphragm setting on the side tube was f16. On the other limb of the beam splitter we connected a cine adaptor (301 587) focal length F = 107 together with a C thread mount containing a Spectrotech SE5 barrier filter in its upper aperture. A Beaulieu R16 cine camera was fitted to the C thread mount and correctly oriented (Fig. 1). This was driven by a rechargeable

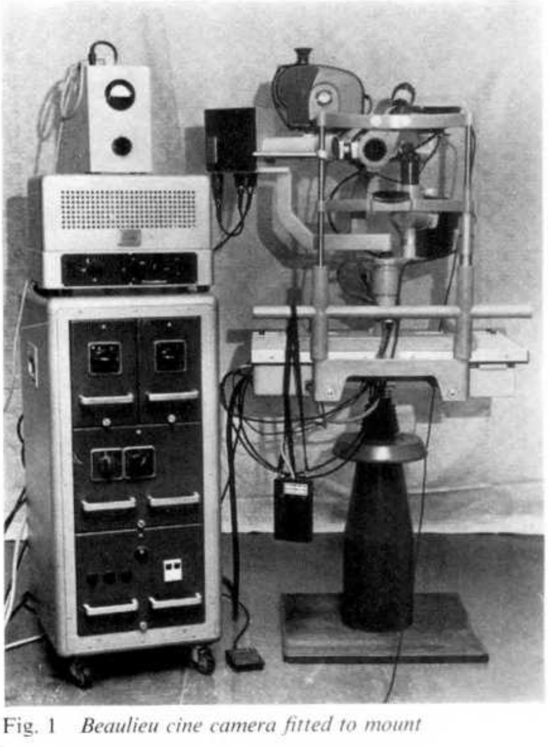
Fig. 1 *Beaulieu cine camera fitted to mount*

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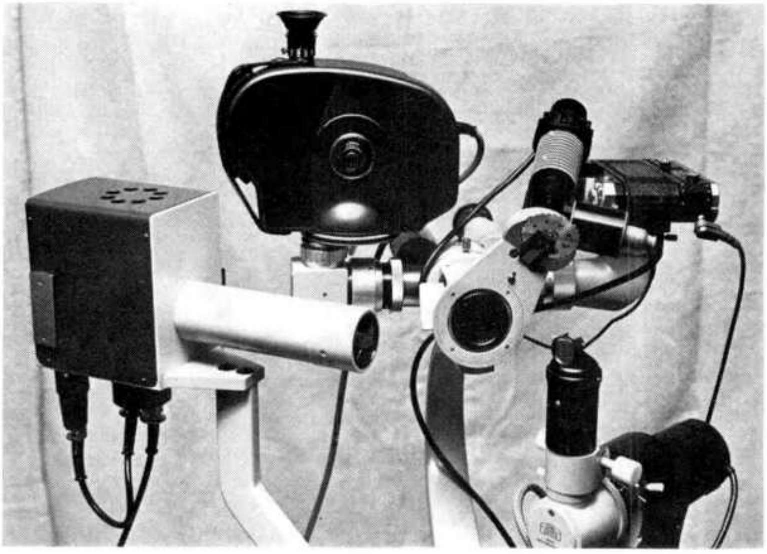

Fig. 2 *Equipment for illumination*

battery pack and was fired by manual control. The aperture on the camera support was set at f7 and the cine camera set at 12 frames per second. We found that with this combination the whole of the iris could be encompassed in one frame of the cine film. An Ilford 109 gelatin filter was cut out and fitted into 1 of the eyepieces so that fluorescence could be directly observed.

The sources of illumination were twofold. The slit beam aperture was fully opened and set at 9, and covered by a Spectrotech exciter filter SB4 of 7 mm diameter. In front of it was opposed a −4·0 sphere lens of the same diameter. This was effective in increasing the field of illumination to encompass the whole iris. An additional halogen iris fluorescence lamp driven by an accessory power source (Carl Zeiss Oberkochen 120 VA power supply unit) was fitted on a central spindle of the photo-slit lamp and a Spectrotech exciter filter SE4 was fitted in the appropriate holder (Fig. 2). The magnification settings were as follows: for iris angiograms we found × 16 to be optimal and with sectoral corneal abnormalities × 25. When the machine was ready we injected 5 ml of 20% fluorescein into an antecubital vein, and after 6 seconds the cine camera was started. The footpedal was depressed and the flash fired when fluorescein was first seen entering the anterior segment. We found that we were able to take 12 exposures at 1·5 second intervals. After this time it took a further 13 to 14 seconds for the starter to be charged for another flash.

The film used in the Nikon camera was Ilford HP5 and that in the cine camera was 16 mm Kodak Eastman 4-X negative film 7224. The 35 mm HP5 film was processed using D 76 developer for 20 minutes at 80°F (27°C). The cine film was processed in a methol-hydroquinone developer of D76 standard and forced developed by one stop. It was best projected at 12 frames per second and observed in greater detail 1 frame at a time by using a Carl Zeiss Jena documator with the 16-mm reel adaptors.

We have also adapted the technique for television monitoring. The cine camera is substituted by a CCTV (Hitachi HV 40 SU) miniature television camera. The diaphragm on the side tube was set at f11, otherwise all settings were identical to those used for cine. We viewed the angiogram on a Hitachi 75-square-inch (484-cm²) picture video monitor VM 126AU (EK) and recorded the dye transit on a video tape recorder (National Panasonic NV 5120A).

We found that cine photography gave the best definition and single frame analysis, the best quality of all coinciding with the flash exposure on the film. The major disadvantage was the slow speed of projection required, which limited us to a small number of cine projectors, though there was also the possibility of double printing each frame of the film. We found cine film expensive, and there was a delay in the developing and printing. Video tape recording, on the other hand, can be viewed immediately, conveniently, and repeatedly during and after recording. It is especially useful for studying the vascular pattern of a lipid keratopathy prior to laser occlusion. Surprisingly, we found patients remarkably good at tolerating the very bright illumination necessarily produced by this system.

References

Bron, A. J., and Easty, D. L. (1970). Fluorescein angiography of the globe and anterior segment. *Transactions of the Ophthalmic Societies of the United Kingdom*, **90**, 339–367.

Brun-Jensen, J. (1969). Fluorescein angiography of the anterior segment. *American Journal of Ophthalmology*, **67**, 842–845.

Chignell, A. H., and Easty, D. L. (1971). Iris fluorescein photography following retinal detachment and in certain ocular ischaemic conditions. *Transactions of the Ophthalmic Societies of the United Kingdom*, **91**, 243–357.

Cobb, B. (1968). Vascular tufts at the pupillary margin. *Transactions of the Ophthalmic Societies of the United Kingdom*, **88**, pp. 211–212.

Jensen, V. A., and Lundback, K. (1968). Fluorescence and angiography of the iris in recent and long term diabetics. Congress XVIII Ophthal. septentr. Copenhagen, 1967, *Acta Ophthalmologica*, **46**, 584–585.

Kottow, M. (1976). *Iris angiography in vascular diseases of the fundus. Documenta Ophthalmologica*, **9**, 465–471.

Laatikainen, L., and Blach, R. K. (1977). Behaviour of the iris vasculature in central retinal vein occlusion: a fluorescein angiographic study of the vascular response of the retina and iris. *British Journal of Ophthalmology*, **61**, 278–284.

Mapstone, R. (1970). Ischaemia in vein occlusions. *British Journal of Ophthalmology*, **54**, 312–315.

Marsh, R. J., Easty, D. L., and Jones, B. R. (1974). Iritis and iris atrophy in ophthalmic zoster. *American Journal of Ophthalmology*, **78**, 255–260.

Mitsui, Y., Matsubara, M., and Kanawaga, M. (1969). Fluorescence irido-corneal photography. *British Journal of Ophthalmology*, **53**, 505–512.

Raitta, C., and Vannas, S. (1969). Fluoreszein Angiographie der Irisgefasse nach Zentralvenenverschluss. *Albrecht von Graefes Archiv für klinische und experimentelle Ophthalmologie*, **177**, 33–38.

Vannas, A. (1969). Fluorescein angiography of the vessels of the iris in pseudo exfoliation of the lens capsule, capsular glaucoma and some other forms of glaucoma. *Acta Ophthalmologica*, Suppl. 105, pp. 24 et seq.

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Penetration of tobramycin sulphate into the human eye

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SUMMARY Tobramycin sulphate, a new aminoglycoside antibiotic, was injected intramuscularly (80 and 100 mg) and subconjunctivally (10 mg) into patients, and the concentrations of the drug in serum and aqueous humour were determined 1 hour after the injection by an agar wall diffusion plate method. The intramuscular administration of tobramycin produced insignificant and noninhibitory concentrations in the aqueous humour, while therapeutically effective levels of the antibiotic appeared in the aqueous after subconjunctival administration of tobramycin (mean: 18·9 μg/ml). These data suggest that tobramycin sulphate may be of value in the treatment of ocular infections.

Aminoglycosides are broad spectrum antibiotics widely used in the treatment of ocular infections and for postoperative prophylaxis. Tobramycin sulphate is a new water-soluble, parenterally administered antibiotic of the aminoglycoside group, derived from *Streptomyces tenebarius.* Its chemical structure, kinetics, pharmacodynamics, and antimicrobial properties closely resemble those of gentamicin (Bodey and Stewart, 1972; Dienstag and New, 1972). It has been proved that tobramycin is more effective than gentamicin against pseudomonas strains *in vitro* (Traub and Raymont, 1972; Levison and Kaye, 1974; Wretlind and Gezelius, 1976), and it has been reported that it seems to be less toxic than gentamicin (Federspil, 1974). The peak serum concentration of tobramycin occurs between 30 and 90 minutes after intramuscular administration, and detectable levels persist for as long as 6 to 8 hours (Goodman and Gilman, 1975). There is some information on the intraocular penetration of tobramycin in rabbits (Purnell and MacPherson, 1974; Uwayadah and Faris, 1976), but the penetration of the antibiotic into the human eye after administration by various routes has not yet been reported.

The present study was carried out to determine the concentration of tobramycin sulphate in the serum and aqueous humour of patients after intramuscular and subconjunctival administration of the antibiotic.

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Patients and methods

Thirty-one patients, aged 58 to 82 years, scheduled for routine cataract extraction under local anaesthesia were selected for this study. All had a normal anterior segment on clinical examination and none of them had a history of drug allergy, renal disease, or any other contraindications to tobramycin administration.

The patients were divided into 3 groups as follows: In the first group each one of 9 patients was given 80 mg of tobramycin in a single intramuscular injection; in the second group each of 7 patients was given 100 mg in a single intramuscular dose; in the third group each of 15 patients was given 10 mg of tobramycin subconjunctivally in the eye to be operated upon. The eye was anaesthetised with benoxinate 0·4% eye drops, and 0.25 ml (10 mg) of the tobramycin solution was injected subconjunctivally in the inferior half of the globe by means of a tuberculin syringe with a 27 G needle. The patients in all 3 groups received the antibiotic 1 hour before operation. The eyes were prepared for routine cataract extraction. On the operating table, after retrobulbar anaesthesia, lid block, and conjuctival flap dissection, a keratome making a 3 mm incision was inserted in the anterior chamber at 12 o'clock. Simultaneously a tuberculin syringe with a 25 G needle was introduced into the chamber below the keratome and 0·2 ml of aqueous humour was aspirated. At the same time a venous sample (4 to 5 ml) was also collected. The operation was continued in routine fashion. The blood and

Table 1 *Human serum and aqueous humour tobramycin levels in μg/ml 60 minutes after a single intramuscular injection (80 mg in group I and 100 mg in group II) and a single subconjunctival injection of 10 mg of tobramycin (group III)*

Subjects	*Group I*		*Group II*		*Group III*	
	Serum	*Aqueous*	*Serum*	*Aqueous*	*Serum*	*Aqueous*
1	2·0	0·7	3·1	0·4	1·15	17
2	2·8	0·2	5·2	1·6	1·10	20
3	5·0	0·2	4·2	1·3	1·15	15
4	1·5	0·3	11·0	1·9	0·57	16
5	2·8	0·8	6·0	0·2	0·40	20
6	9·0	0·2	11·0	2·6	0·36	18
7	5·0	0·3	8·4	1·4	0·38	22
8	5·2	0·2			0·78	17
9	3·3	0·2			1·40	19
10					0·80	23
11					0·50	12
12					1·12	21
13					0·90	20
14					0·42	24
15					0·20	20
Mean	4·07± 2·28	0·30± 0·26	6·9± 3·21	1·34± 0·8	0·74± 0·37	18·9± 3·17

aqueous samples, packed in ice, were delivered within 1 hour to the laboratory for antibiotic assay.

ASSAY METHOD

The antibiotic concentration in serum and aqueous humour was determined by an agar wall diffusion plate method (Bennett *et al.*, 1966). Petri dishes contained a base agar layer (pH 6·8), overlaid with a seeded layer prepared with a suspension of *Bacillus subtilis* NCTC 8236 as test organism. Small holes (4·5×2·5 mm) were opened and filled with samples. All samples were run in duplicate. Using standard concentrations of six different tobramycin solutions a standard curve was plotted on semilog paper. The diameter zones were measured in millimetres by a microestimator after 24 hours of incubation at 37°C. Concentrations of the antibiotic were determined in μg/ml by reading the concentration directly from the standard curve derived stimultaneously from the similarly prepared known concentration of antibiotic diluted in human serum and saline.

Results

The concentrations of tobramycin sulphate found in the aqueous humour and serum 1 hour after intramuscular and subconjunctival antibiotic administration are listed in Table 1 and are shown in Fig. 1 schematically.

Group I. A single intramuscular injection of 80 mg of tobramycin resulted in a mean serum level of 4·072±2·28 μg/ml and a mean aqueous concentration of 0·3±0·26 μg/ml.

Group II. 100 mg of tobramycin injected intramuscularly produced a mean serum concentration of 6·94±3·2 μg/ml and an average aqueous humour level of 1·33±0·8 μg/ml.

Group III. Sixty minutes after a single subconjunctival dose of 10 mg (0·25 ml) of tobramycin sulphate the mean antibiotic serum level was 0·74±0·37 μg/ml and the average tobramycin aqueous concentration was 18·9±3·17 μg/ml.

All the patients had a normal postoperative course and none showed any anterior segment changes resulting from the subconjunctival injection of tobramycin.

Discussion

The treatment of ocular infections caused by Gram-negative bacteria, and especially by *Pseudomonas aeruginosa* strains, cannot be regarded as satis-

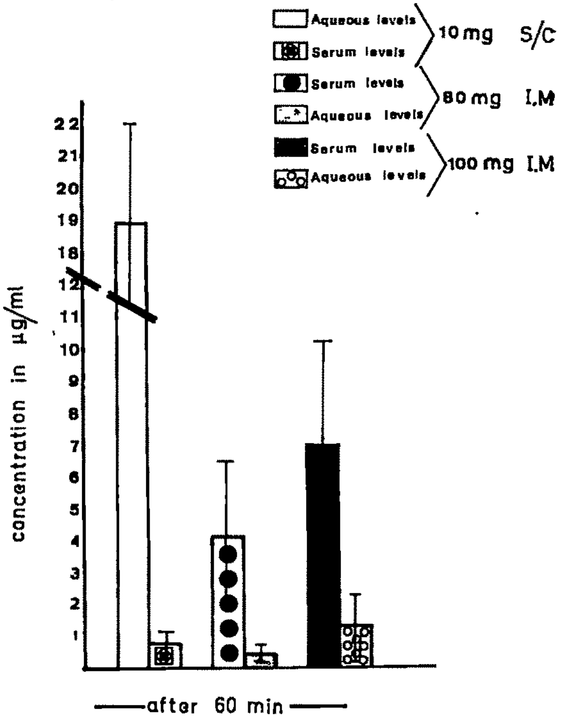


Fig. 1 *Mean serum and aqueous humour tobramycin levels following intramuscular and subconjunctival injection in man*

factory. Tobramycin sulphate is a new antibiotic of the aminoglycoside group that seems to be more effective, at least *in vitro*, against these bacteria, as reported previously. Our results show that tobramycin penetrates the eye poorly after intramuscular injection, while therapeutically effective concentrations in the aqueous humour resulted from subconjunctival administration.

The intramuscular injection of tobramycin in a single dose of 80 mg produced aqueous levels of the antibiotic (0·3±0·26 μg/ml) which are much lower than the minimum inhibitory concentration for the majority of the pathogenic bacteria (Jaffe *et al.*, 1974). When 100 mg of tobramycin was injected intramuscularly, the antibiotic level produced in the aqueous fluid (1·33±0·8 μg/ml) was 4 times higher than that produced by the intramuscular injection of 80 mg. This antibiotic level in the aqueous can be effective against some bacteria, but undesirable side effects may be produced by a dose of 100 mg of tobramycin. The inability of tobramycin to penetrate the normal human eye in therapeutic levels was expected and is consistent with published data on other aminoglycosides to which tobramycin is related (Litwak *et al.*, 1969; Furgiuele, 1970; Maclwain *et al.*, 1974). When 10 mg of tobramycin was injected subconjunctivally, the antibiotic level produced 1 hour after administration was much higher than the minimum inhibitory concentration of all the pathogenic bacteria, even *Pseudomonas* species (Jaffe *et al.*, 1974). The levels of antibiotic obtained in the aqueous after subconjunctival injection are higher than those of other antibiotics of the same group (Furgiuele, 1970; Maclwain *et al.*, 1974). The variations in the mean values of tobramycin aqueous levels observed in our experiments are consistent with other data on tobramycin and other aminoglycosides (Litwak *et al.*, 1969; Uwaydah and Faris, 1976).

Finally, we can conclude that tobramycin levels in the aqueous humour obtained from subconjuctival administration were sufficient to inhibit all strains of pathogenic bacteria, while an efficient barrier prevents the diffusion of tobramycin from serum to the primary aqueous humour of the normal human eye. The intramuscular administration of the antibiotic produces subtherapeutic levels in the aqueous humour.

References

Bennett, J., Brodie, J., Benner, E., and Kirby, W. (1966). Simplified, accurate method for antibiotic assay of clinical specimens. *Applied Microbiology*, 14, 170–178.

Bodey, C., and Stewart, D. (1972). In vitro studies of tobramycin. *Antimicrobial Agents and Chemotherapy*, 2, 109–113.

Dienstag, J., and New, H. (1972). In vitro studies of tobramycin, an aminoglycoside antibiotic. *Antimicrobial Agents and Chemotherapy*, 1, 41–45.

Federspil, P. (1974). Experimental and clinical studies on the ototoxitity of tobramycin. In: *Tobramycin, Selected Proceedings from the Eighth International Congress of Chemotherapy, Athens, September* 1973, pp. 38–43. Excerpta Medica: Amsterdam.

Furgiuele, F. P. (1970). Penetration of gentamycin into the aqueous humor of human eyes. *American Journal of Ophthalmology*, 69, 481–483.

Goodman, L., and Gilman, A. (1975). In *The Pharmacological Basis of Therapeutics*, 5th edn., pp. 1175–1176. Macmillan: New York.

Jaffe, G., Ravreby, W., Meyers, B., and Hirschman, S. (1974). Clinical study of the use of the aminoglycoside tobramycin for therapy of infections due to Gram negative bacteria. *Antimicrobial Agents and Chemotherapy*, 5, 75–81.

Levison, M. E., and Kaye, D. (1974). In vitro comparison of four aminoglycoside antibiotics: sisomicin, gentamycin, tobramycin and BBK8. *Antimicrobial Agents and Chemotherapy*, 5, 667–669.

Litwak, K. Petit, T., and Johnson, B. (1969). Penetration of gentamycin administrated intramuscularly and subconjunctivally into aqueous humor. *Archives of Ophthalmology*, 82, 687–693.

MacIlwaine, W., Sande, M., and Mandel, G. (1974). Penetration of antistaphylococal antibiotics into the human eye. *American Journal of Ophthalmology*, 77, 589–592.

Purnell, W., and McPherson, S. (1974). The effect of tobramycin on rabbit eyes. *American Journal of Ophthalmology*, 77, 578–582.

Traub, W., and Raymond, E. (1972). Evaluation of the in vitro activity of tobramycin as compared with that of gentamicin sulfate. *Applied Microbiology*, 23, 4–7.

Uwaydah, M., and Faris, B. (1976). Penetration of tobramycin sulfate in the aqueous humor of the rabbit. *Archives of Ophthalmology*, 94, 1173–1174.

Wretlind, B., and Gezelius, L. (1976). Sensitivity of isolated *Pseudomonas aeruginosa* to amikacin, gentamicin, sisomicin and tobramycin. *IRCS, Journal of Medical Science*, 4, 156.

Book reviews

Fortschritte der Kiefer- und Gesichts-Chirurgie. Vol. 22. Periorbitale Chirurgie. Anomalien, Krankheiten und Geschwülste der Gefässe. Edited by KARL SCHUCHARDT and RÜDIGER BECKER. 1977. Pp. 225, figs., tables, refs. Georg Thieme Verlag, Stuttgart (DM238)

The product of many contributors, this book (in German) deals with the classification, causes, diagnosis, and treatment of orbital and periorbital problems. It covers the subject fully but sometimes in a rather superficial manner.

Some chapters are of greater interest than others, for example, that on the use of miniplates in the reconstruction of the orbital margin. Others treat their subjects loosely, as in the articles dealing with ptosis. The search for the perfect, universally acceptable procedure for correcting ptosis continues, but only 2 cases are cited by the author of the paper on the use of the frontalis muscle taken through the frontal sinus to simulate the more natural line of pull of the upper lid. There is a section dealing with late reconstruction of the orbit using Silastic implants. Satisfactory results are reported with the use of the magnetic implant. The section dealing with craniofacial abnormalities suffers from having to follow the high standard set by Tessier. The article dealing with basal cell carcinoma claims that there is less recurrence if the lesion was not previously radiated or surgically treated, and the claim is substantiated on the basis of 426 cases. Haemangiomata receive attention with the claim that cryotherapy is satisfactory for small lesions but only palliative for larger ones.

This is an interesting book, up to date, easily readable, if one is fluent in German. The references are good but not complete, and refer mainly to the European literature, so that they may be helpful especially to those readers who are not familiar with it.

A. WEBB

Die therapeutische Anwendung von ionisierenden Strahlen in der Augenheilkunde. By P. LOMMATZSCH. 1977. Pp. 148, figs., refs. Georg Thieme, Leipzig (DDR 27)

The scope of radiotherapy in ophthalmology has undergone considerable contraction in the past 20 years, largely as a result of the development of medical measures for effectively dealing with many of the chronic non-neoplastic lesions encountered, coupled with the important advances that have taken place in the surgery of neoplasms arising in relation to the eye. In these circumstances it is refreshing to welcome a book on the use of ionising radiation in the treatment of diseases of the eye and its related structures.

The authors, of whom the senior, Dr Lommatzsch, is a well-known ophthalmologist, all practise in East Berlin, and the range of subjects covered and the standards set do them the utmost credit. Approximately half the book is devoted to an account of the physical and biological bases of radiotherapy, including sections on protection and radiation technique. The section on physics is detailed, thorough, and up to date, covering electron beam therapy, neutron therapy, and treatment by linear accelerators. It is interesting to note that the radiation doses are quoted in the newly proposed Gray unit, which has not been generally adopted in Britain (1Gy = 100 rads). The amount of information contained in this section will probably prove daunting to the average ophthalmologist but should impress the radiotherapist. The section on technique covers treatment by x rays ranging from low voltage to megavoltage, gamma and beta ray therapy, and electron beam therapy. The authors mention the methods they themselves use and illustrate where applicable the apparatus developed by them, but the whole chapter is so condensed and overlaid with relevant references to other workers that there are no clear indications or details of the precise technique the authors would recommend when using a particular piece of equipment for a particular lesion. A similar criticism can be levelled at the chapter on the treatment of individual tumours affecting the eye, orbit, lids, and epibulbar region, namely, there is a concentration on references with no clear picture of what the authors themselves recommend. There is an adequate chapter on the radiosensitivity of the occular and adnexal tissues and a most interesting chapter on the use of radiation in inflammatory and non-malignant lesions of the eye. The latter chapter is of course mostly of historical interest, but it is still worth perusing if only for this reason.

The book is well produced and illustrated and contains a remarkably complete and up-to-date bibliography. It should prove of great value as a reference book for any ophthalmologist or radiotherapist interested in this special field.

M. LEDERMAN

Drugs and the Eye. By JANET VALE and BARRY COX. 1978. Pp. 126, figs., tables. Butterworth, London (£5·50)

This book is designed to be a detailed and yet concise account of drugs and their use in the eye and to be a working guide for qualified ophthalmic opticians. It opens with a chapter on anatomy and physiology and then discusses factors affecting drug absorption. Cycloplegics, mydriatics, miotics, local anaesthetics, staining agents, antimicrobial agents, solutions used in contact lens work, and anti-inflammatory compounds all have chapters of their own. The ocular effects of drugs used systemically are discussed. There is a chapter on first aid and emergency measures used by ophthalmic opticians. The final 2 sections are on formulation of eye preparations and the legal aspects of sale and supply of drugs. The physiology of neurohumoural transmission and the receptor theory of drug action is particularly well described, and indeed there is much to interest the practising ophthalmologist in this relatively short textbook of 126 pages.

S. J. H. MILLER

Obituary

J. S. Charamis, MD

Greece and ophthalmology have lost one of their leading medical personalities in the death of Professor John S. Charamis at the age of 73. He was born and brought up in Athens, where his father was an eminent ophthalmologist, and received his higher education in Athens and Paris. He finally settled in Athens to follow his father's professional career and early in life became well known as a pioneer of modern Greek ophthalmology.

Professor Charamis was scrupulous in all he undertook. He was the founder and director of the ophthalmic department at the Greek Red Cross Hospital, Athens (1933–47). In 1931 he founded the Hellenic Ophthalmological Society and in 1947 was elected professor in ophthalmology at Athens University and director of Ophthalmiatrion Eye Hospital. In 1970 he was elected a member of the Athens Academy in recognition of his scientific achievements. He made a valuable contribution to the successful campaign against trachoma in Greece and he was awarded the gold medal of the League against Trachoma in 1961.

An outstanding teacher, Professor Charamis will always be remembered for his agile mind and the ability to express himself concisely and cogently. He was a hard worker throughout his life and organised his time to the demands of a busy private practice, the burden of administration in the medical faculty, the clinical work in his hospital, and the increasing obligations of his international commitments.

His academic achievements at home and abroad were many. From 1952 he was a member of the International Council of Ophthalmology and its president from 1966 to 1970. In 1967 he was elected a member of the Academy of Athens, the highest academic distinction in Greece. He was a foreign member of the Académie de Médecine de Paris from 1973 and a member of the Academy of Rome from 1976. Among the many medals he was awarded were the Médaille d'or des lettres, arts et sciences de la ville de Paris, the Helmholtz medal, the Médaille de l'union Médical Balkanique, and the Médaille Favarolo. He published 370 scientific papers and a successful book on eye surgery (1943).

Charamis conceived the idea of a national institute of ophthalmology to house the university clinics and realised his aim after 10 years of sustained work. He was interested in a wide range of subjects, mainly history and art. A stimulating companion during his leisure hours, he always made visitors welcome, and many colleagues from all parts of the world will retain the memory of the warm and generous hospitality received at the hands of John Charamis and his charming wife, Angela. He was a gentle and kind man with great personal charm and dignity. He is survived by his wife, a son, and daughter.

J. TSAMPARLAKIS

Notes

Intraocular implants

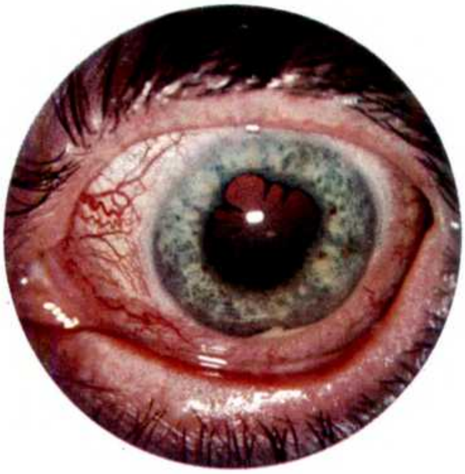
An international congress and film festival on intraocular implants, organised by the French Intraocular Implant Society, will be held at the Palais des Festivals in Cannes on 2–5 May 1979. The principal theme of the congress will be 'The physiological basis of intraocular implantation'. The official langages will be French and English with simultaneous translation. Further details from: Dr L. Amar, Palais Armenonville, 06400 Cannes, France. Phone: (93) 38 31 28.

Clinical electrophysiology

The International Society for Clinical Electrophysiology of Vision will hold its 17th symposium in Schloss Reinhardsbrunn, Friedrichroda, German Democratic Republic, on 5–10 June 1979. Two topics have been selected: 'Visual electrodiagnosis in systemic diseases' and 'Visual electrophysiology and localised retinal stimulation'. The official language is English. Further information from: Professor Dr E. Schmöger, Augenklinik der Medizinische Akademie, Nordhäuserstrasse 74, 50 Erfurt, GDR.

International congress of ophthalmology

The European Society of Ophthalmology will hold its sixth Congress on 21–25 April 1980 in the Brighton Centre under the patronage of the Duke of Gloucester. The main theme is the study of the cornea in health and disease. The president of the Organising Committee is Mr Desmond P. Greaves, of the Moorfields Eye Hospital, London. Secretary-General of the Scientific Programme is Professor W. S. Foulds, of the Tennent Institute of Ophthalmology, University of Glasgow. Secretary-General for the organisational matters is Mr John E. Wright, of the Moorfields Eye Hospital, London. Further information from: Holland Organising Centre, 16 Lange Voorhout, 2514 EE The Hague, The Netherlands.



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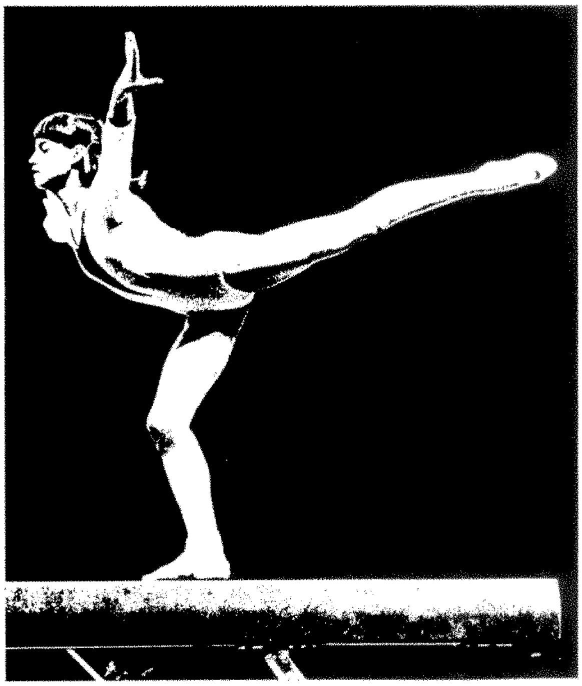

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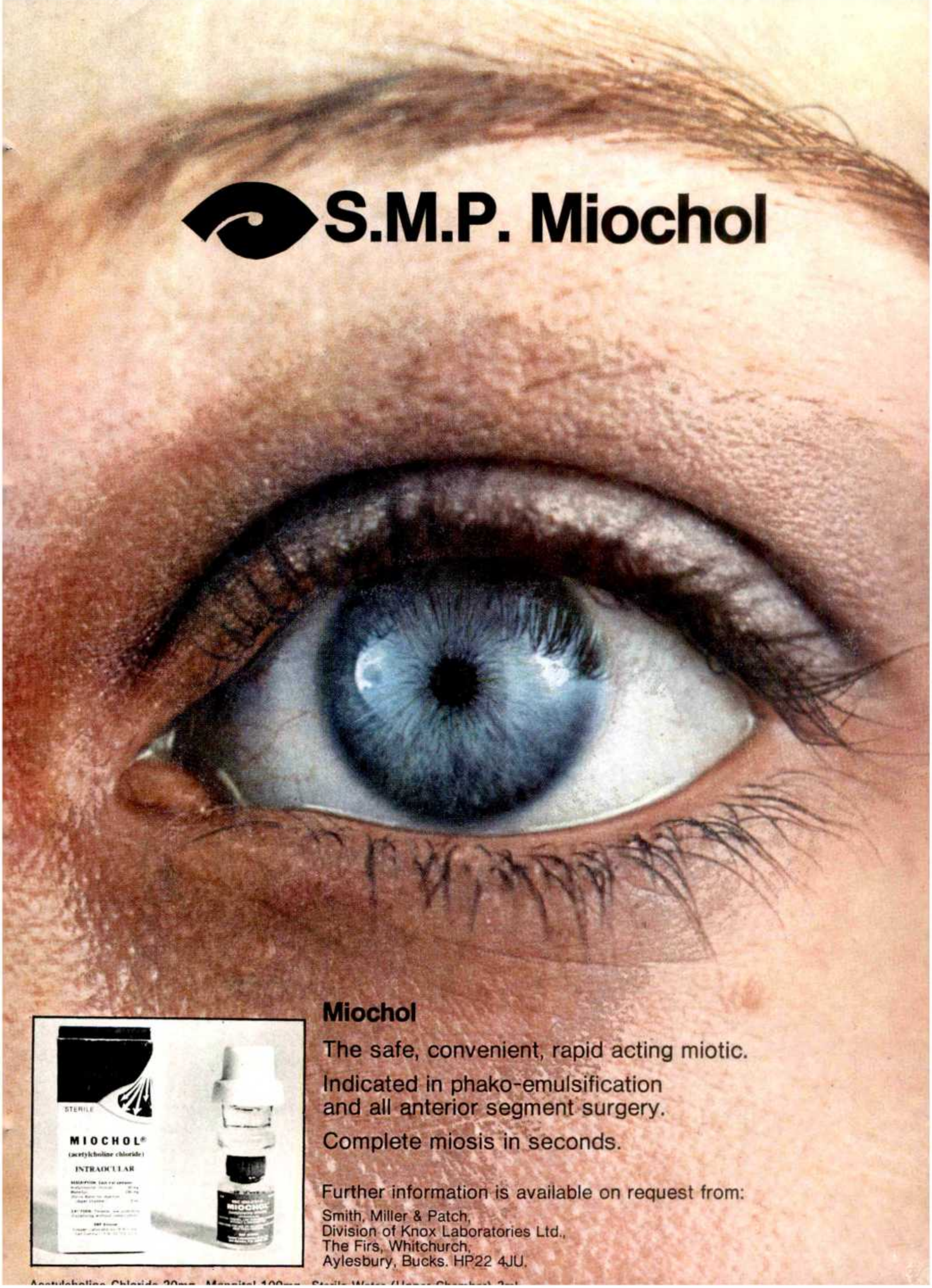

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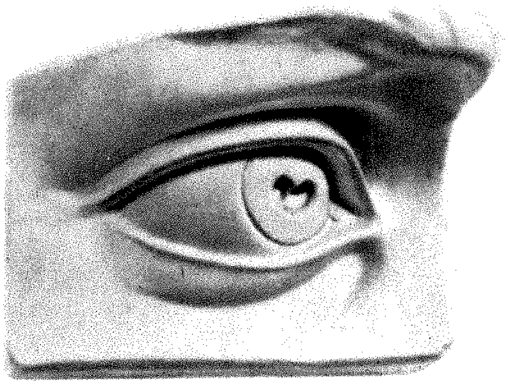

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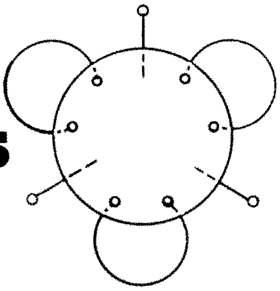

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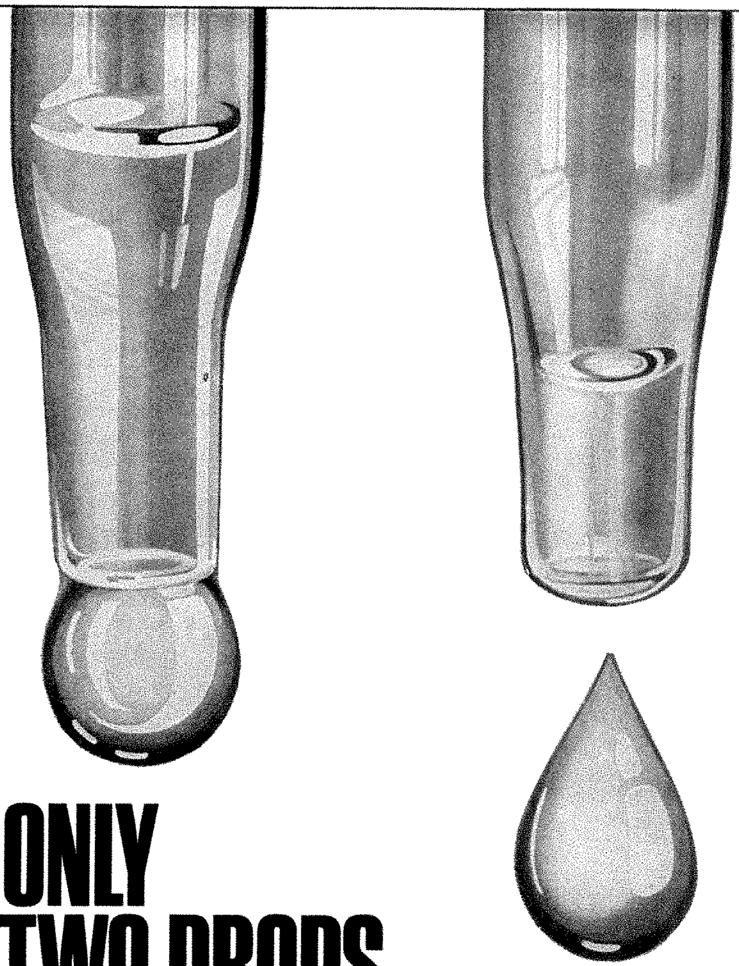

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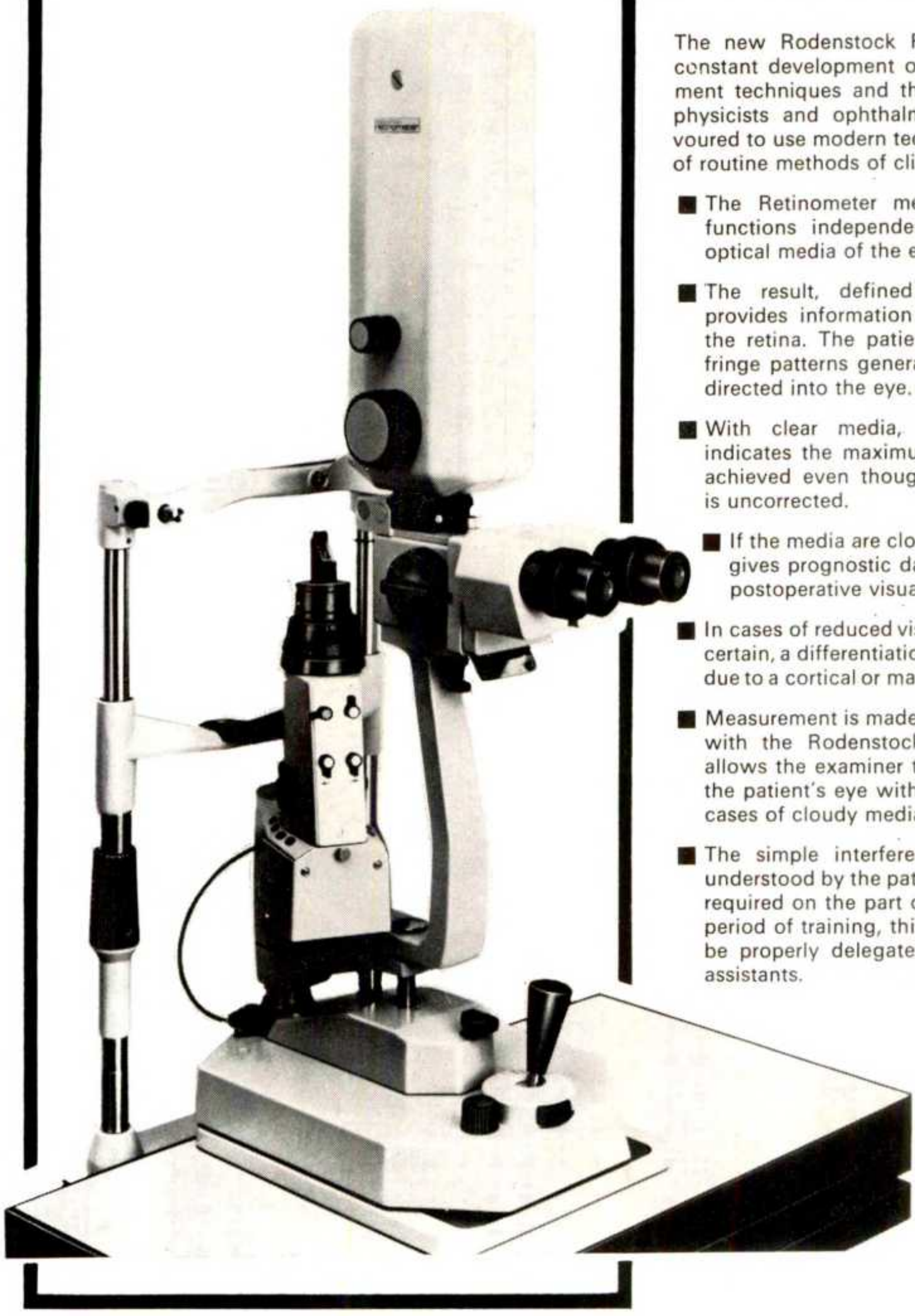

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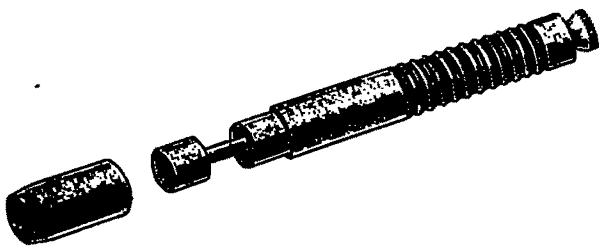

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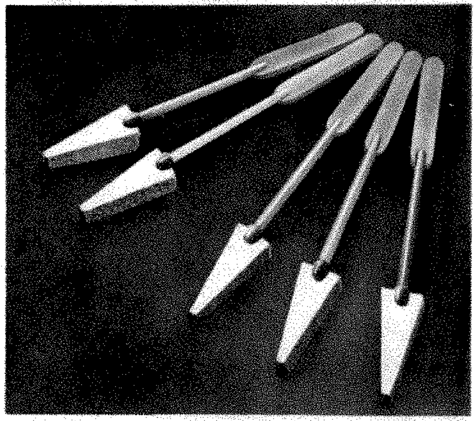

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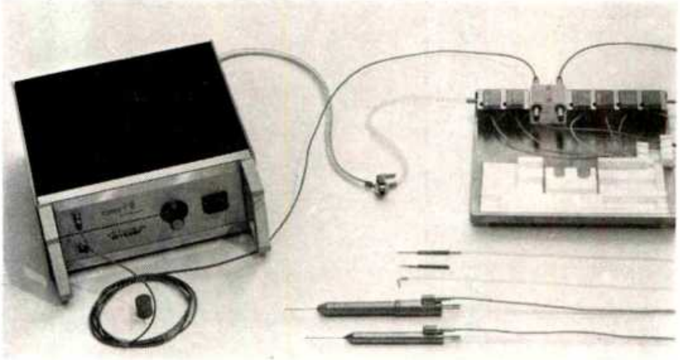

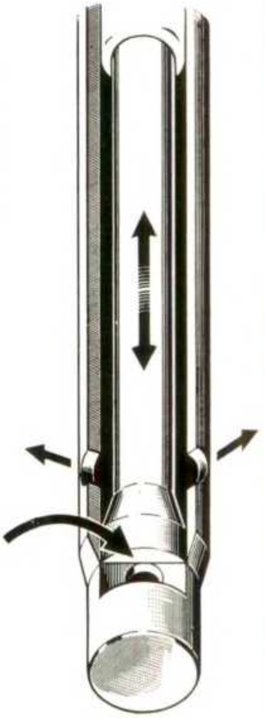

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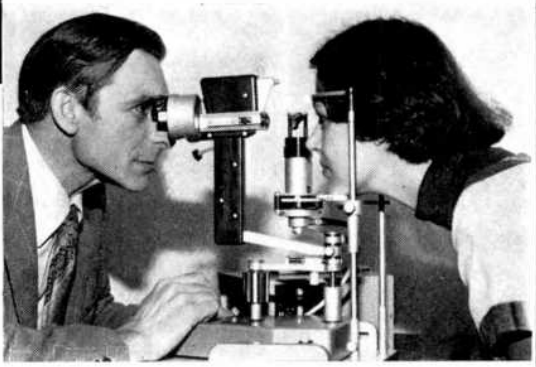

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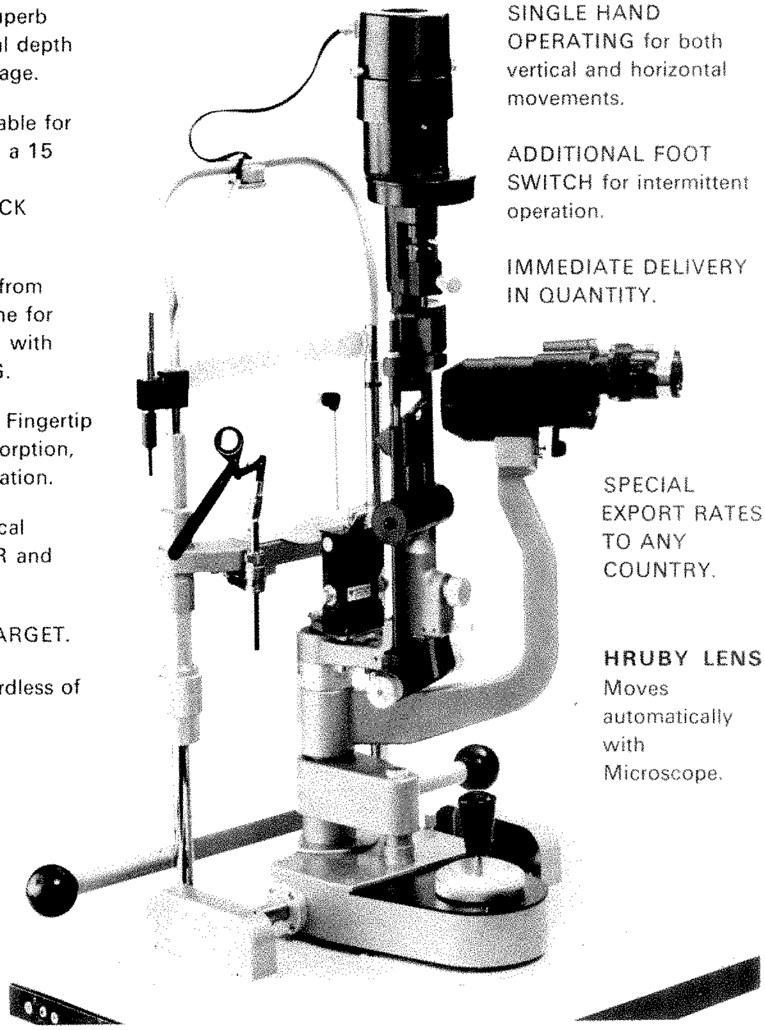

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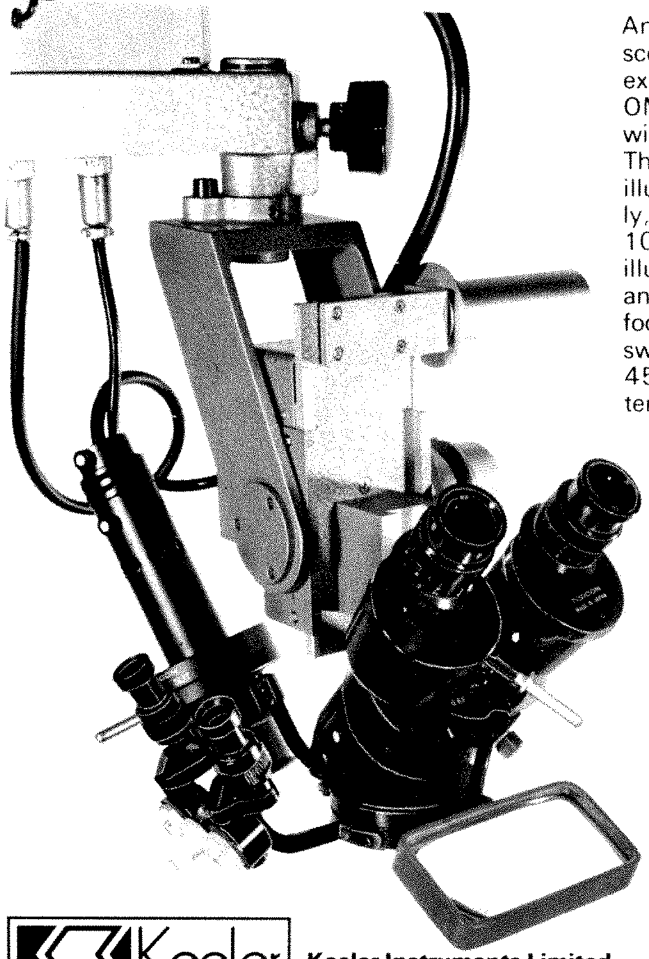

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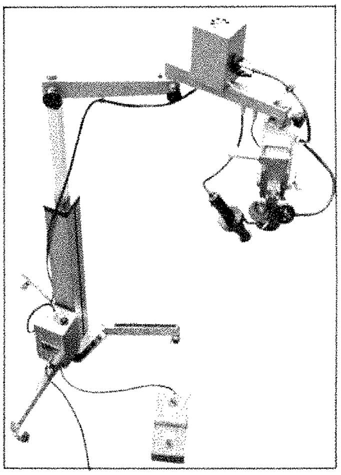

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British Journal of Ophthalmology, 1978, **62**, 665–669

Quantitative relationship between cupping of the optic disc and visual field loss in chronic simple glaucoma

J. GLOSTER

From the Institute of Ophthalmology, London

SUMMARY The extent of cupping was measured from optic disc photographs of 300 patients with ocular hypertension and suspected or established chronic simple glaucoma, and their visual fields were recorded. The incidence of field defects increased as the vertical cup:disc ratio increased, a value of 0·70 for this ratio being a particularly useful guide to the presence or absence of field loss. There was a significant correlation between the extent of cupping and the size of the visual field. The vertical cup:disc ratio was the most useful quantitative index of cupping.

The decision that cupping of the optic disc is pathological rather than physiological is of great importance in the diagnosis of chronic simple glaucoma. Sometimes this decision is difficult, and it is then helpful to correlate the result of a visual field examination, which must always be done, with the appearance of the disc. If it is thought, for example, that the edge of the cup is abnormally near to the edge of the disc in the inferotemporal sector, then the finding of an early upper arcuate scotoma supports the view that the cupping is pathological. In addition to a topographical relationship between disc damage and field loss, one may also attempt the more difficult judgment of whether the amount of glaucomatous cupping matches the amount of field loss. In practical clinical terms one tries to answer the question whether the visual field loss can be wholly accounted for by glaucoma, or whether some additional pathology has to be considered.

The relationship between glaucomatous damage to the optic nerve head and visual field loss has been examined in various ways: (1) By relating a particular feature of the disc to the presence or absence of a field defect or to the position or progression of the defect. The features of the disc which have received attention include the size and shape of the cup, pallor and notching of the neuroretinal rim, and haemorrhages (Chandler and Grant, 1965; Armaly, 1969, 1970; Read and Spaeth, 1974; Drance, 1975; Gloster, 1975; Hitchings and Spaeth, 1977; Drance *et al.*, 1977). (2) By correlating the extent of glaucomatous cupping of the disc with the amount of field loss. In one study (Fisher *et al.*, 1970) the extent of cupping was graded and the field loss was measured, while in another study (Gloster, 1976) cup:disc ratios were measured and the field loss was divided into 4 grades.

The purpose of the present paper is: (1) to determine the incidence of demonstrable glaucomatous field defects at various values of the vertical cup:disc ratio; (2) to correlate the amount of field loss with quantitative expressions of glaucomatous damage to the disc.

Methods

PATIENTS

All the information used was derived from fundus photography and visual field examinations which formed part of the routine investigation of patients attending the Glaucoma Clinic at the Institute of Ophthalmology, London. The patients were either glaucoma suspects, cases of ocular hypertension, or established cases of chronic simple glaucoma, and all had shown at some time an intraocular pressure greater than 20 mmHg.

FUNDUS PHOTOGRAPHY AND MEASUREMENTS OF CUPPING OF THE OPTIC DISC

These procedures have been fully described in previous papers (Gloster and Parry, 1974; Gloster, 1975). The cup:disc ratios used in the present study are: (1) the vertical cup:disc ratio, that is, the vertical diameter of the cup divided by the vertical diameter of the disc; (2) the horizontal cup:disc ratio, that is, the analogous ratio of the horizontal

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diameters; (3) the area ratio that is, the area of the cup divided by the area of the disc; (4) the rim: diameter ratio, that is, the narrowest part of the rim of the cup divided by the diameter of the disc.

VISUAL FIELD TESTING

Each patient was examined in three ways: (1) The central field was tested with the Globuck screen (Buchanan and Gloster, 1965). This presents stimuli as flashes in 74 fixed positions in the central field. The extent of the field was expressed as the number of stimuli seen by the patient. (2) The central field was also examined on the Goldmann perimeter with the 1:4 stimulus presented as a flash in 188 fixed positions as described by Gloster (1970). Again, the number of stimuli seen was used to express the extent of the field. (3) The peripheral and central fields together were tested on the Goldmann perimeter by kinetic perimetry with the 1:4 stimulus. The area of seeing field as plotted on the chart was measured by means of a planimeter.

Results

INCIDENCE OF GLAUCOMATOUS FIELD DEFECTS AT VARIOUS VALUES OF THE VERTICAL CUP:DISC RATIO

Table 1 summarises the findings for 300 eyes. In 150 eyes there was no associated field defect, these results relating either to patients with ocular hypertension or to those with chronic simple glaucoma with unilateral field loss. In the remaining 150 eyes there was glaucomatous field loss. Table 1 shows that there was a particularly rapid increase in the incidence of field defects when the vertical cup:disc ratio attained a value of about 0·70. If this value was used to separate eyes which would be expected to show a glaucomatous field defect from those which would not, it was found that a correct separation could be made for 87% of the eyes. The accuracy with which the vertical cup:disc ratio could be measured depended greatly on the certainty with which the position of the edge of the cup could be defined. When the disc photographs were measured, a note was made of whether the observer was certain, fairly certain, or doubtful of the position of the cup edge. It should be emphasised that this was a matter not of the quality of the photograph but of the actual appearance of the disc, and this conforms to the common clinical experience that in some discs it is easy to say how much is cupped while in others it is difficult. Table 2 shows how certainty or uncertainty about the edge of the cup affected the use of a cup:disc ratio of 0·70 for separating eyes with field defects from those with full fields. It is clear that doubt about the cup edge had a marked effect. When there was no doubt about the extent of cupping, use of the vertical cup: disc ratio allowed a correct statement to be made about the presence or absence of a field defect in 94% of eyes.

Table 1 *The incidence of glaucomatous field defects at various values of the vertical cup:disc ratio*

Vertical cup: disc ratio	*Incidence of field defect*
	(%)
0·90–0·99	100
0·80–0·89	95
0·70–0·79	65
0·60–0·69	20
0·50–0·59	4
0·40–0·49	6
0·30–0·39	0

300 eyes: 150 with field defects. 150 with full fields.

Table 2 *The effect of uncertainty about the position of the cup edge on the use of the vertical cup:disc ratio for separating eyes with field defects from those with full fields*

Position of cup edge	*No. of eyes*	*Correct separation*
		(%)
Certain	131	94
Fairly certain	84	87
Doubtful	85	78

Table 3 *Mean vertical cup:disc ratios for eyes with full fields and for eyes with early, intermediate, and glaucomatous field loss*

Field loss	*Mean vertical cup: disc ratio*
None n=150	0·57
Early n=50	0·76
Intermediate n=50	0·80
Advanced n=50	0·88

CORRELATION OF FIELD LOSS WITH CUP:DISC RATIOS

Table 3 gives the mean vertical cup:disc ratios for the same group of 300 eyes as in Table 1. 150 eyes had full fields (and an intraocular pressure >20 mmHg) and 150 had glaucomatous field loss. According to the severity of the field loss a division could be made into three subgroups: (1) 50 eyes with an early defect consisting of a paracentral or arcuate scotoma; (2) 50 eyes with an intermediate defect consisting of an arcuate scotoma breaking

Table 4 *The correlation of disc measurements and visual fields*

	Correlation coefficients			
	Vertical cup:disc ratio	*Horizontal cup:disc ratio*	*Area cup:disc ratio*	*Rim:diameter ratio*
Goldmann perimeter, central and peripheral field together, kinetic method	–0·69	–0·55	–0·66	0·56
Globuck screen, central field, static method	–0·68	–0·62	–0·68	0·60
Goldmann perimeter, central field only, static method	–0·79	–0·55	–0·67	0·69

out to the periphery with loss of a nasal quadrant; (3) 50 eyes with an advanced defect, in which a small central island remained, sometimes together with a temporal island. It can be seen that there was a progressive increase in the mean vertical cup:disc ratio as the visual field became smaller.

In order to investigate further the relationship between the size of the cup and the amount of field loss, results were analysed from 40 eyes with field loss, in all of which there was no doubt about the position of the whole of the edge of the cup. Only 1 eye from each patient was included in this analysis. Correlation coefficients were calculated between the size of the visual field and the vertical and horizontal cup:disc ratios, the area ratio, and the rim:diameter ratio; the values obtained are given in Table 4 and all were highly significant ($P<0·001$). By contrast, the maximum untreated intraocular pressures for this group of patients showed no significant correlation with field loss ($P=0·152$). In the case of the vertical, horizontal, and area cup:disc ratios the correlation with the size of the visual field was negative, as would be expected, because the larger the cup the greater the field loss. The correlation was positive for the rim:diameter ratio because the narrower the rim the greater the incidence of field loss.

From Table 4 it can be seen that: (1) the best correlation was between the vertical cup:disc ratio and the central field obtained on the Goldmann perimeter by the static method; (2) the field loss was more closely related to the vertical cup:disc ratio than to the horizontal cup:disc ratio, there being a significant difference ($P<0·05$) between the two correlation coefficients (–0·79 and –0·55) for the central Goldmann field.

Figs. 1 and 2 show the relationship of the vertical and horizontal cup:disc ratios to the size of the visual field. In each case the linear regression line has been drawn, although it is an assumption that the relationship is linear. The greater scatter of the horizontal ratios than of the vertical ratios can be seen.

Discussion

The results given show that in general the size of the cup in an optic disc can be related quantitatively to the incidence and extent of glaucomatous field loss, although there is a wide variation which limits the application of this quantitative relationship to the individual patient.

It is of interest to note from Table 3 that there is a considerable increase in the vertical cup:disc ratio in eyes with early glaucomatous field defects as compared with eyes which had intraocular pressures over 20 mmHg but full fields. This observation supports the idea that it is useful to undertake periodic photography of the optic disc in the supervision of cases of ocular hypertension because it suggests that enlargement of the cup could be detected before a scotoma became evident.

The view previously expressed that the vertical cup:disc ratio is more useful clinically than the horizontal cup:disc ratio (Gloster and Parry, 1974; Gloster, 1975) receives further support from the study of the correlation of these ratios with the extent of field loss (see Table 4 and Figs. 1 and 2). It is possible to use the vertical cup:disc ratio to differentiate, with a fair degree of accuracy, between discs which are associated with a glaucomatous field defect (that is 'glaucomatous' discs) from those which are associated with full fields (that is, 'probably non-glaucomatous' discs). The efficiency of this method of recognising glaucomatous discs depends on the certainty with which the upper and lower edges of the cup can be recognised. The practical outcome of these results is that when the judgment has to be made with the ophthalmoscope as to whether cupping is physiological or pathological special attention should be paid to the upper and lower margins of the cup. If there is uncertainty about the edges of the cup, the pupil should be dilated (with due regard to the width of the angle), and the disc should be examined with the slit-lamp and Hruby or fundus contact lens. If a reasonably accurate estimate of the vertical cup:disc ratio can

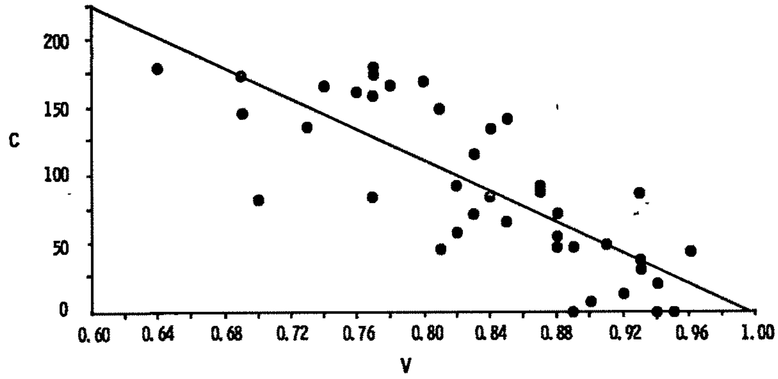

Fig. 1 *The relationship between the size of the visual field and the vertical cup: disc ratio. Ordinate: C = number of stimuli seen in central field on Goldmann perimeter. Abscissa: V = vertical cup: disc ratio*

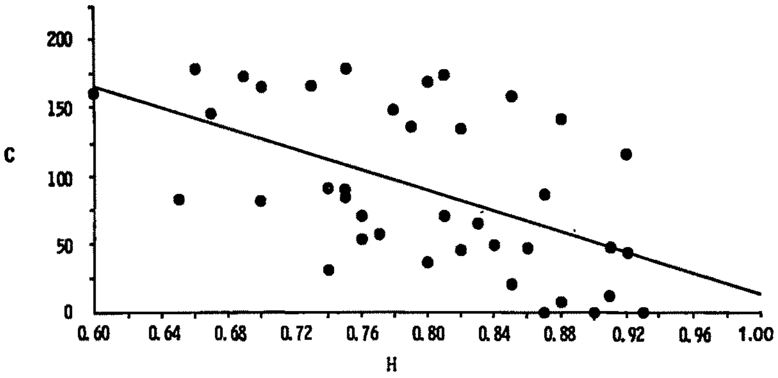

Fig. 2 *The relationship between the size of the visual field and the horizontal cup: disc ratio. Ordinate: as in Fig. 1. Abscissa: H = horizontal cup: disc ratio*

be made (and this is often possible from ophthalmoscopic or slit-lamp examination), the data in Table 1 give an indication of the probability that the disc is or is not glaucomatous.

If the data of Table 1 are translated into clinical probabilities and applied to eyes with tensions greater than 20 mmHg, the following can be said: (1) If the vertical cup:disc ratio is less than 0·4, there is a very low probability that the disc is glaucomatous. (2) With values of the ratio between 0·4 and 0·6, the chances are about 1 in 20 that the disc is glaucomatous. (3) When the ratio is between 0·6 and 0·7 the chances are 1 in 5 that the disc is glaucomatous. (4) At a value of about 0·7 for the vertical cup:disc ratio there is a very rapid increase in the chances that a disc is glaucomatous. (5) When the ratio is between 0·7 and 0·8, the chances are 2 to 1 that the disc is glaucomatous, rising to almost 20 to 1 for ratios between 0·8 and 0·9. (6) When the ratio exceeds 0·9 the disc is certainly glaucomatous.

The factor of variation allows us to make a statement of probability only, but in this respect we are in the same situation as with measurements of intraocular pressure and their relationship to the diagnosis of glaucoma, except that observations on the disc are more closely related to loss of visual function than are measurements of intraocular pressure. Quite apart from giving a more precise statement of the probability of glaucomatous change in the individual patient, the vertical cup: disc ratio may be of use in research projects as a quantitative objective index of the stage to which glaucoma has progressed.

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References

Armaly, M. F. (1969). The correlation between appearance of the optic cup and visual function. *Transactions of the American Academy of Ophthalmology and Otolaryngology*, 73, 898–913.

Armaly, M. F. (1970). Optic cup in normal and glaucomatous eyes. *Investigative Ophthalmology*, 9, 425–429.

Buchanan, W. M., and Gloster, J. (1965). Automatic device for rapid assessment of the central visual field. *British Journal of Ophthalmology*, **49**, 57–70.

Chandler, P. A., and Grant, W. M. (1965). *Lectures on Glaucoma*, Chapter 1. Kimpton: London.

Drance, S. M. (1975). Correlation of optic nerve and visual field defects in simple glaucoma. *Transactions of the Ophthalmological Societies of the United Kingdom*, **95**, 288–296.

Drance, S. M., Fairclough, M., Butler, D. M., and Kottler, M. S. (1977). The importance of disc haemorrhage in the prognosis of chronic open angle glaucoma. *Archives of Ophthalmology*, **95**, 226–228.

Fisher, R. F., Carpenter, R. G., and Wheeler, C. (1970). Assessment of established cases of chronic simple glaucoma. *British Journal of Ophthalmology*, **54**, 217–228.

Gloster, J. (1970). Flash perimetry. *British Journal of Ophthalmology*, **54**, 649–658.

Gloster, J. (1975). Vertical ovalness of glaucomatous cupping. *British Journal of Ophthalmology*, **59**, 721–724.

Gloster, J. (1976). In: *Recent Advances in Glaucoma*. Edited by S. Rehak and G. Paterson. International Glaucoma Symposium, Prague, 1976. Springer-Verlag: Berlin.

Gloster, J., and Parry, D. G. (1974). Use of photographs for measuring cupping in the optic disc. *British Journal of Ophthalmology*, **58**, 850–862.

Hitchings, R. A., and Spaeth, G. L. (1977). The optic disc in glaucoma. II: Correlation of the appearance of the optic disc with the visual field. *British Journal of Ophthalmology*, **61**, 107–113.

Read, R. M., and Spaeth, G. L. (1974). The practical clinical appraisal of the optic disc in glaucoma: the natural history of cup progression and some specific disc-field correlations. *Transactions of the American Academy of Ophthalmology and Otolaryngology*, **78**, 255–274.

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The optic disc in glaucoma, III: diffuse optic disc pallor with raised intraocular pressure

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SUMMARY Ten patients (14 eyes) with chronic simple glaucoma are described, each with features atypical for this disease and more suggestive that each had suffered an acute ischaemic optic neuropathy. Diagnosis of an acute ischaemic optic neuropathy in these cases is important, as treatment of ocular hypertension in the contralateral 'normal' eye may prevent a similar attack.

Optic nerve disease and visual loss in chronic simple glaucoma probably occur as a result of several different mechanisms. Sudden field loss following an acute ischaemic optic neuropathy may be only one of them.

A close relationship between the appearance of the optic disc in glaucomatous eyes and the presence or absence of visual field loss has been emphasised in recent years (Armaly, 1969; Douglas *et al.*, 1974; Hoskins and Gelber, 1975; Hitchings and Spaeth, 1977). Visual field defects of a nerve fibre bundle type have been found to coexist with changes at the neuroretinal rim at the site of the nerve fibres presumed to be involved. Hitchings and Spaeth (1977) divided these changes at the affected part of the neuroretinal rim into thinning or absence of the rim with or without obvious pallor. The decrease in the width of the rim was associated with an increase in the vertical cup/disc ratio, and if *not* associated with 'pallor' might or might not have had an associated field defect. 'Pallor' of the neuroretinal rim was found in conjunction with visual field defects and would be localised to the area of the rim considered to correspond with the defect in the visual field. Hitchings and Spaeth (1977) found these signs adequate to identify field loss correctly in over 80% of eyes with glaucoma. Few eyes in the remaining 20% did not, in retrospect, show localised changes at the neuroretinal rim.

This paper reports on 10 patients (14 eyes), each with an intraocular pressure greater than 21 mmHg and glaucomatous cupping, most with 'nerve fibre bundle' field defects, in which the optic disc did not show the expected localised changes. It is suggested that each of these eyes had suffered an acute ischaemic optic neuropathy, and, although by definition each eye had chronic simple glaucoma, the process by which visual loss occurred may well differ from that occurring in 'typical' chronic simple glaucoma showing localising signs at the optic disc.

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Materials and methods

The 10 patients, aged 50 to 80 years, mean 66·5 years, were referred for evaluation of their glaucoma. Each had been discovered to have 'glaucomatous cupping', intraocular pressures greater than 21 mmHg at the time of referral to the author, and, in 11 of the 14 eyes, glaucomatous visual field defects. Each was subjected to a full ophthalmic examination. Each eye had an open angle on gonioscopic examination. Visual field examinations were performed with a Goldmann perimeter. In each case this visual field examination was supplemented by specific confrontation field testing to look for a central scotoma by means of simultaneous presentation of 2 identical red-coloured targets, 1 each to central and paracentral fields. Mydriasis and slit-lamp biomicroscopy of the posterior segment were performed in each case. Evaluation of the optic disc and retinal nerve fibres followed the method described by Hitchings and Spaeth (1976).

The colour of the neuroretinal rim of each optic disc was noted to be either pink or pale. Colour estimation was made by examining the disc with a slit beam of light and then comparing the appearance of one sector of the rim (say, inferotemporal) with other sectors of the same optic disc as well as the corresponding sector of the contralateral optic disc. By this means diffuse (uniform) pallor or localised pallor of the neuroretinal rim could be appreciated.

Table 1 *Summary of results*

Patient number	*Age at presentation*	*Presenting symptoms*	*Acuity at presentation*		*Intraocular pressure at presentation*		*Optic disc appearance*	*Vertical C/D*		*Visual field*
			Right	*Left*	*Right*	*Left*		*Right*	*Left*	
1	80	*LEV ↓ ×6/12	6/6	6/12	26	28	R and L. Pale disc with circular cups, retinal nerve fibres not seen	0·8	0·8	R. Full L. Central scotoma and inferior arcuate defect
2	74	*REV ↓ ×5/52	6/24	6/12	31	24	R and L. Pale disc with circular cups. Retinal nerve fibres not seen	0·4	0·2	R. Central scotoma with temporal field loss L. Inferior visual field loss
3	77	LEV ↓ ×6/12	6/5	6/18	18	26	R. Pink disc with visible retinal nerve fibres L. Pale disc with circular cup	0·7	0·8	R. Full L. Central scotoma
4	61	REV ↓ ×12/12	6/9	6/6+	45	40	R and L. Pale disc with circular cups. Retinal nerve fibres not seen	0·7	0·6	R. Central scotoma with inferior altitudinal field loss L. Inferior altitudinal field loss
5	60	LE Pain ×3/32	6/9	6/18	21	24	R. Pink disc with circular cup and visible nerve fibres L. Pale disc with circular cup, retinal nerve fibres not seen	0·3	0·5	R. Full field L. Central scotoma with upper arcuate defect
6	66	REV ↓ ×6/12	6/12	6/6	56	40	R. Pale disc with circular cup L. Pale disc with vertically oval cup. Retinal nerve fibres not seen	0·8	0·8	R. Central scotoma L. Paracentral scotoma in upper field
7	65	LEV ↓ ×3/12	6/6	6/9	18	40	R. Pink disc, visible retinal nerve fibres L. Pale disc with circular cup, retinal nerve fibres not seen	0·4	0·8	R. Full field L. Inferior arcuate defect
8	72	LEV ↓ ×2/12	6/6	6/9	20	30	R. Pink disc, visible retinal nerve fibres L. Pale disc with circular cup, retinal nerve fibres not seen	0·1	0·5	R. Full field L. Inferior altitudinal defect
9	50	Amaurosis fugax R eye	6/9	6/9	14	14†	R. Disc pale, retinal nerve fibres not seen L. Pink disc with circular cup and visible retinal nerve fibres	0·7	0·4	R. Central scotoma L. Full field
10	52	LEV ↓ ×6 days	6/9	6/18	16	16†	R and L. Pale optic disc with circular cups. No retinal nerve fibres seen	0·5	0·4	R and L. Inferior nasal defect

* LEV: Left eye vision. * REV: Right eye vision. † Patients subsequently developed raised intraocular pressure

Results

The results are summarised in Table 1. Of the 10 patients 8 presented with (central) visual loss. (In 6 of these patients symptoms had been present for months, and referral to hospital was initiated by the optician on detection of depressed central acuity unaccounted for by refractive errors.) Fourteen of the 20 eyes had diffuse pallor of the optic disc together with a circular orifice of the optic cup. Five eyes had pink optic discs with small central cups and were considered normal. One eye (the left eye of Patient 7) had a vertically oval cup in an atrophic disc considered typically glaucomatous. No patient had aphakia or marked nuclear sclerosis to alter colour appreciation of the optic disc.

Five patients had bilateral disc pallor. The orifice of the optic cup was circular for all except the left eye of Patient 7. In each case the vertical cup-to-disc ratio was similar in the 2 eyes, not differing by more than 0·2 C/D for any patient. The other 5 patients had 1 optic disc considered normal, the other showing diffuse pallor with a circular orifice to the optic cup (Figs. 1, 2). This group of patients exhibited a greater disparity in vertical cup-to-disc ratios between the 2 eyes, the C/D ratio of the normal optic disc being equal to or smaller than the C/D ratio of contralateral pale disc (see Table 1).

No retinal nerve fibres could be seen in any of the eyes showing diffuse pallor of the neuroretinal rim, whereas an apparently intact retinal nerve fibre layer could be seen in those eyes with a pink optic disc.

The best corrected visual acuity at presentation to the author was found to be less than 6/6 in at least 1 eye in every patient. This visual defect could not be accounted for by opacities in the optical media. No patient had a manifest squint or gross aneisometropia to suggest amblyopia.

Visual field defects were found only for the eyes with pale optic discs. Eight of these eyes had defects in the lower half of the visual field, while a central scotoma to red was found in 7 eyes. Two eyes had defects in the upper half of the visual field and 1 eye with diffuse pallor of the optic disc had no detectable field defect (see Table 1).

Patient 10 presented to the hospital with a 6-day history of diminished vision in his left eye. Examination of the left eye at that time revealed a swollen optic nerve head; a diagnosis of acute ischaemic optic neuropathy was made (Fig. 3). Raised intraocular pressure was not found until 2½ years after the initial presentation, at which point the patient was referred to the author. Examination at that time revealed bilateral optic disc pallor with circular cups, having a vertical C/D ratio of 0·5 and 0·4 in the right and left eye (Fig. 4).

Discussion

The points raised by the cases presented in this paper may be conveniently discussed under three headings. Firstly, the similarities and differences between these cases and 'typical' chronic simple glaucoma. Secondly, the similarities between these cases and 'typical' cases of ischaemic optic neuropathy. Thirdly, the relationship of elevated intraocular pressure to ischaemic optic neuropathy.

SIMILARITIES AND DIFFERENCES BETWEEN THE CASES PRESENTED AND 'TYPICAL' CHRONIC SIMPLE GLAUCOMA

The optic disc in the normal eye is circular or vertically oval (Tomlinson and Phillips, 1974) while the orifice of the optic cup is circular or horizontally oval (Portnoy, 1973). The retinal nerve fibres may be seen as lines radiating from the disc. The arcuate fibres are most easily seen adjacent to the upper and lower temporal quadrants of the optic disc. Visual field loss in glaucoma is associated with a vertical enlargement of the orifice of the optic cup (Kirsch and Anderson, 1973; Weisman, A. *et al.*, 1973; Portnoy, 1975) following loss of neurones and glia from the neuroretinal rim (Anderson, 1975).

Patients with 'typical' chronic simple glaucoma with visual field loss limited to the upper or lower half show localised thinning of the lower or upper half of the neuroretinal rim. In addition pallor of the same part of the rim and a defect in the adjacent part of the nerve fibre layer are frequently seen (Hitchings and Spaeth, 1977). Patients presented in this paper had visual loss in the upper or lower field, but did *not* show the expected localised pallor or thinning of the neuroretinal rim or localised defects in the retinal nerve fibre layer. These three features will be discussed separately.

Colour appreciation

Colour appreciation at the optic disc is open to gross observer error. Firstly, diffuse illumination of the posterior fundus (achieved with a direct ophthalmoscope or colour photography), allows 'colour leak' from the peripapillary choroid to the adjacent optic disc, giving a falsely pink appearance to pale disc tissue (Gloster, 1971).

Illumination of the optic disc without the peripapillary choroid, by means of a narrow beam of light, allows more accurate colour appreciation by limiting colour leak (Gloster and Parry, 1974). The narrow light beam allows colour comparisons to be made between corresponding areas of the neuroretinal rim above and below the horizontal meridian of the optic disc, or nasal and temporal to the vertical meridian. By limiting these colour differences to 'pink' or 'pale', gross differences between similar areas (upper temporal sector of the neuroretinal rim and lower temporal sector, etc.) of one or both optic discs of one may be noted (Hitchings and Spaeth, 1976).

The second major source of observer error is the false appreciation of optic disc colour produced by alterations in the optical media of the eye. The light reflected from the eye is affected by the senile lens, which acting as a filter frequently imparts a pinkish hue to the optic disc (Snydacker, 1964; Kronfeldt, 1967). In contrast the optic disc in an aphakic eye seems paler than its fellow seen through a lens. Neither of these two factors was present to affect colour appreciation for the patients in this study.

Slit-lamp biomicroscopy showed diffuse pallor of the affected optic discs in the eyes presented in this paper. In contrast eyes with 'typical' chronic simple

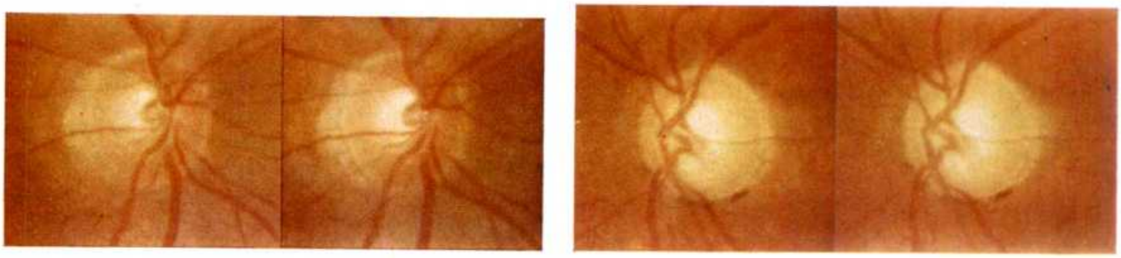


Fig. 1 *Right and left optic disc of Patient 8. The right disc was considered normal, the left disc showed diffuse pallor of the neuroretinal rim and was considered abnormal*

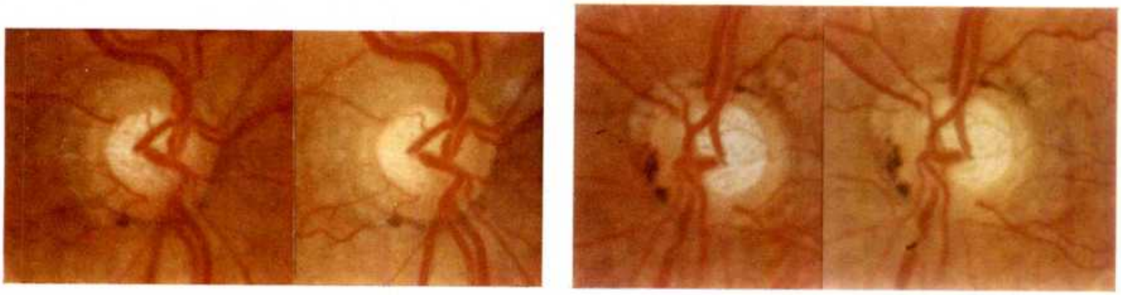
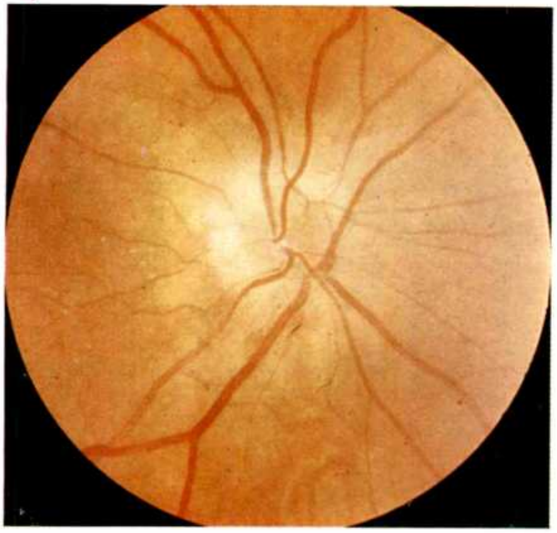


Fig. 2 *Right and left disc of Patient 2. The right optic disc is pink in colour and considered normal; note the large C/D. The left optic disc shows uniform pallor of the neuroretinal rim, a larger C/D ratio with a circular orifice to the optic cup, and was considered abnormal*



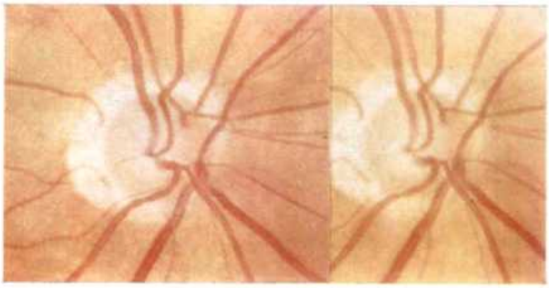


Fig. 4 *Right eye of Patient 10, at presentation to the author. Note depressed optic cup and diffuse pallor of the neuroretinal rim*

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Fig. 3 *Right eye of Patient 10 at the time of presentation with a 'typical' acute ischaemic optic neuropathy. Note swollen nerve head and haemorrhages*

Note: *'Colour leak' (see text) from the peripapillary choroid has made the pallor, where present, less obvious. Intact nerve fibre bundle layers were visible on biomicroscopy in the right eye of Figs. 1 and 2. Figs 1, 2, and 4 are stereo-pairs and should be viewed through a plus sphere suitably decentred* glaucoma have pallor of the neuroretinal rim receiving neurones from the defective visual field (Armaly, 1969; Douglas *et al.*, 1974; Hoskins and Gelber, 1975; Hitchings and Spaeth, 1977). Schwartz (1973) suggested recently that diffuse pallor of the optic disc occurs only in terminal glaucoma, indicating neuronal loss from all parts of the retina together with loss of most of the visual field.

Localised thinning of the neuroretinal rim

Localised thinning of the neuroretinal rim has been shown to be a sign of 'typical' chronic simple glaucoma (Hitchings and Spaeth, 1976). Thinning is most easily identified by stereoscopic biomicroscopy, comparisons being made between the sector of rim in question and the corresponding sector in the other eye *or* the corresponding sector above or below the horizontal in the same eye. The 14 eyes with diffuse pallor did *not* show localised thinning of the neuroretinal rim despite field defects limited in some cases to one upper or lower half of the visual field. In those patients for whom 1 disc, being pink with a small optic cup, appeared normal comparison between the glaucomatous and normal eye showed the neuroretinal rim in the former to be uniformly thinner. As might be expected, cup-to-disc ratios tended to be considerably larger in the abnormal eye.

Nerve fibre bundle defects

Nerve fibre bundle defects have been shown to occur in patients with glaucoma and to coincide with defects in the visual field (Hoyt *et al.*, 1973; Hitchings and Spaeth, 1977). Although many eyes with advanced glaucoma do not have any visible nerve fibre layer notwithstanding the state of the visual field (Hitchings and Spaeth, 1977), eyes having relatively well localised field defects frequently show 'gaps' or 'grooves' in the retinal nerve fibre layer.

None of the eyes with diffuse optic nerve pallor presented in this paper had visible retinal nerve fibres despite visual fields that ranged from 'normal' to an altitudinal field loss. In contrast *all* of the eyes with pink optic discs had an intact retinal nerve fibre layer. The optic discs with diffuse pallor may have suffered loss of sufficient neurones to abolish the reflexes arising from the inner retina, but, apparently, not enough to produce defects detectable by kinetic Goldmann field testing in each part of the visual field.

SIMILARITIES BETWEEN THE CASES PRESENTED AND 'TYPICAL' ISCHAEMIC OPTIC NEUROPATHY

Case 1 was referred to the author 2½ years after bilateral ischaemic optic neuropathy following the later development of raised intraocular pressures. At that time the physical signs were the same as for the other cases presented.

Quigley and Anderson (1978) recently described in a large series the appearance of the optic disc before and after a documented attack of acute ischaemic optic neuropathy. They noted each optic disc developed diffuse pallor. Those optic discs which, before the attack, had small optic cups developed 'flat white discs', while in the much less common eyes in which the optic cup was large *before* the attack the appearance of the disc *after* the attack was that of a pale *cupped* disc—differing from 'typical' chronic simple glaucoma in that the orifice of the optic cup was circular rather than vertically oval. Quigley and Anderson's observation that the optic disc may appear glaucomatous in eyes with large optic cups before an acute ischaemic optic neuropathy agrees with the findings for the cases presented in this paper, where each of the 5 normal fellow eyes had quite large optic cups.

Reviewing the visual field defects in their series of cases of ischaemic optic neuropathy Quigley and Anderson (1978) found defects to exist predominantly either in the inferior half of the visual field or as a central scotoma, whereas in glaucoma the early field defects affect the superior half ot the visual field (Harrington, 1971). Our patients had field defects sited most frequently in the lower half of the visual field and/or a central scotoma.

RELATIONSHIP BETWEEN ELEVATED INTRAOCULAR PRESSURE AND ISCHAEMIC OPTIC NEUROPATHY

Previous reports have associated acute ischaemic optic neuropathy with ocular hypertension. Foulds (1969) on finding raised intraocular pressure in 7 of 24 consecutive cases of ischaemic optic neuropathy emphasised the role of raised intraocular pressure in reducing capillary perfusion at the optic nerve head. A similar role for elevated intraocular pressure in the causation of both anterior ischaemic optic neuropathy and glaucoma was suggested by Hayreh (1974). A relatively minor role for raised intraocular pressure in the causation of acute ischaemic optic neuropathy was suggested by the findings of Ellenberger *et al.* (1973), who found no difference between the intraocular pressure in 48 patients with acute optic neuropathy and an equal number of age and sex matched controls. Similarly, Eagling *et al.* (1974) noted raised intraocular pressure in only 1 of 40 cases with ischaemic optic neuropathy, while Quigley and Anderson (1978) detected raised intraocular pressure in only 5 of their 78 cases. No conclusion can be drawn from the cases presented in this paper because referral to the author depended on the association of raised intraocular pressure and glaucomatous cupping.

Although these more recent studies suggest a minor role for raised intraocular pressure in the production of ischaemic optic neuropathy, it is of importance as a condition relatively easy to treat. The apparently normal second eye of a patient whose first eye suffered an acute ischaemic optic neuropathy may run a greater risk of developing the same condition if the intraocular pressure is raised above normal. Even if such an eye shows no sign of damage from the raised pressure, prophylactic antiglaucoma therapy should be given.

Conclusion

This paper has presented a series of eyes with intraocular pressures greater than 21 mmHg, glaucomatous cupping, and in most instances visual field defects. Although by definition each eye suffered from chronic simple glaucoma, atypical features were present in every case. It is suggested that each eye had suffered an ischaemic optic neuropathy.

It is important to differentiate between acute ischaemic optic neuropathy and 'typical' chronic simple glaucoma. The former causes sudden visual loss in contrast to the gradual visual loss in the latter condition. Both conditions may be bilateral. Although raised intraocular pressure may only be a minor factor precipitating an acute ischaemic optic neuropathy, its discovery in the fellow eye of a patient who has suffered such an acute attack merits topical antiglaucoma treatment, even without evidence that the raised intraocular pressure has damaged the eye, in contrast to ocular hypertensive eyes with 'typical' chronic simple glaucoma in the other eye, when under similar circumstances it is not mandatory to begin prophylactic antiglaucoma treatment.

Optic nerve disease and visual loss in chronic simple glaucoma probably occurs as a result of several different mechanisms. Sudden field loss following an acute ischaemic optic neuropathy may be only one of them.

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References

Anderson, D. R. (1975). Pathogenesis of glaucomatous cupping: a new hypothesis. Symposium on Glaucoma. *Transactions of the New Orleans Academy of Ophthalmology*. Mosby: St. Louis.

Armaly, M. (1969). The correlation between appearance of the optic cup and visual function. *Transactions of the American Academy of Ophthalmology and Otolaryngology*, **73**, 898–913.

Douglas, G. R., Drance, S. M., and Schulzer, M. (1974). A correlation of field and disc changes in glaucoma. *Canadian Journal of Ophthalmology*, **9**, 391–402.

Eagling, E. M., Saunders, M. D., and Miller, S. J. H. (1974). Ischaemic papillopathy. *British Journal of Ophthalmology*, **58**, 990–1008.

Ellenburger, C., Keltner, J. L., and Burde, R. M. (1973). Acute optic neuropathy in older patients. *Archives of Neurology*, **28**, 182–185.

Foulds, W. S. (1969). Visual disturbances in systemic disorders, otpic neuropathy and systemic disease. *Transactions of the Ophthalmological Societies of the United Kingdom*, **89**, 125–146.

Gloster, J. (1971). Some recent work in glaucoma. *Proceedings of the Royal Society of Medicine*, **64**, 938–952.

Gloster, J., and Parry, D. G. (1974). The use of photographs for measuring cupping in the optic disc. *British Journal of Ophthalmology*, **58**, 850–862.

Harrington, D. O. (1971). *The Visual Fields*, 3rd edn., pp. 186. Mosby: St. Louis.

Hayreh, S. S. (1974). Pathogenesis of cupping of the optic disc in glaucoma. *British Journal of Ophthalmology*, **58**, 863–876.

Hitchings, R. A., and Spaeth, G. L. (1976). The optic disc in glaucoma, I: Classification. *British Journal of Ophthalmology*, **60**, 778–785.

Hitchings, R. A., and Spaeth, G. L. (1977). The optic disc in glaucoma, II: Correlation of the appearance of the optic disc with the visual field. *British Journal of Ophthalmology*, **61**, 107–113.

Hoskins, H. D., and Gelber, E. C. (1975). Optic disc topography and visual field defects in patients with increased intraocular pressure. *American Journal of Ophthalmology*, **80**, 284–292.

Hoyt, W. F., Frisen, L., and Newman, N. (1973). Fundoscopy of the nerve layer in glaucoma. *Investigative Ophthalmology*, **12**, 814–829.

Kirsch, R. C., and Anderson, D. R. (1973). Identification of the glaucomatous disc. *Transactions of the American Academy of Ophthalmology and Otolaryngology*, **77**, 143–156.

Kronfeldt, P. C. (1967). The optic nerve. Symposium on glaucoma. *Transactions of the New Orleans Academy of Ophthalmology*, Chapter 3. Mosby: St. Louis.

Portnoy, G. L. (1973). Qualitative parameters of the normal optic nerve head. *American Journal of Ophthalmology*, **76**, 655–659.

Portnoy, G. L. (1975). Photogrammatic analysis of volume asymmetry of the optic nerve cup in normal, hypertensive and glaucomatous eyes. *American Journal of Ophthalmology*, **80**, 52–58.

Quigley, H. A., and Anderson, D. R. (1978). Cupping of the disc in ischaemic optic neuropathy. *Transactions of the American Academy of Ophthalmology and Otolaryngology*, **83**, 755–762.

Schwartz, B. (1973). Cupping of the optic disc. *Archives of Ophthalmology*, **89**, 272–276.

Snydacker, D. (1964). The normal optic disc. *American Journal of Ophthalmology*, **58**, 958–963.

Tomlinson, A., and Phillips, C. I. (1974). Ovalness of the optic cup and disc in the normal eye. *British Journal of Ophthalmology*, **58**, 543–549.

Weisman, R. L., Asseff, C. F., Phelps, C. D., Podos, S. M., and Becker, B. (1973). Vertical elongation of the optic cup in glaucoma. *Transactions of the American Academy of Ophthalmology and Otolaryngology*, **77**, 157–163.

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Ocular hypertension: a comparative follow-up of black and white patients

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SUMMARY Forty-four eyes in 25 black patients are compared with 92 eyes of 47 white patients in a population with ocular hypertension followed up for 1 to 12 years in a glaucoma clinic. The black patients present at a younger age than the whites and their mean initial intraocular pressure is significantly higher. The fact that more black ocular hypertensives developed glaucoma—8 eyes (18·1%) in the black population as compared with 5 eyes (5·4%) in the white population—is attributed to these two differences.

Well documented evidence has been recorded on differences in glaucoma among the races. These differences include: age of onset (Luntz, 1972; Monteiro de Gandt and Maertens, 1973; Clarke, 1973), general incidence (Neumann and Zaubermann, 1965; Mann, 1972; Clarke, 1973), the prevalence of the various types of glaucoma (Luntz, 1973), and the natural history of the disease (Neumann and Zaubermann, 1965; Monteiro de Gandt and Maertens, 1973).

Recently we have reported on the long-term follow-up of patients with ocular hypertension, of whom 10·2% developed glaucoma during the follow-up period (David *et al.*, 1977). In the present study we are reporting on the differences between white and black patients with ocular hypertension.

Patients and methods

All the patients attended the glaucoma clinics at the Johannesburg teaching hospitals. The criteria for the diagnosis of ocular hypertension and inclusion in the study are identical to those described in a previous report (David *et al.*, 1977).

Forty-seven white patients (92 eyes) and 25 black patients (44 eyes) with ocular hypertension were followed up for 1 to 12 years. All patients were seen at 2 to 6 month intervals, the intraocular pressure (IOP) was recorded on every visit, and the optic disc was examined. Visual fields were tested with the Goldmann perimeter on every occasion, and a Bjerrum tangent screen was performed once or twice a year. Only patients who attended regularly and were followed up for more than 1 year are included in the study.

Results

The average follow-up time was 47 months for the white patients and 39 months for the blacks.

The mean age of presentation for white patients with ocular hypertension was 65·7 years and for black patients 53·1 years. The mean initial intraocular pressure (mean of 3 readings) and standard deviations for each group are plotted according to each decade of age in Fig. 1. While the highest pressures were measured between 40 and 59 years of age, the number of patients among the white ocular hypertensives increased constantly with age.

Seven black patients (8 eyes) developed glaucoma as compared with 4 (5 eyes) from the group of white patients. In 12 eyes pathological cupping of the disc and glaucomatous visual field defects appeared between 12 and 60 months after the initial diagnosis of ocular hypertension, while in only 1 eye the glaucoma developed as late as 79 months after ocular hypertension was diagnosed. Fig. 2 illustrates the relationship between the mean of the initial 3 intraocular pressure readings in each eye (untreated) and the follow-up time for each eye in months, indicating also those eyes which developed glaucoma in both population groups.

The distribution of the mean initial intraocular pressures in the 2 groups and the relationship between this and the development of glaucoma is seen in Table 1. In both white and black patients

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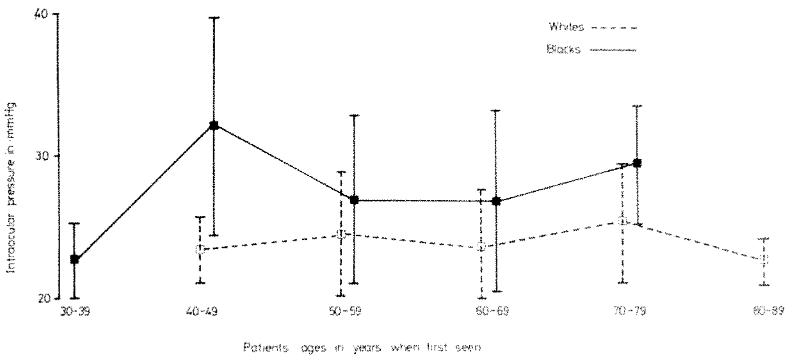
Fig. 1 *Variation of mean IOP with age*



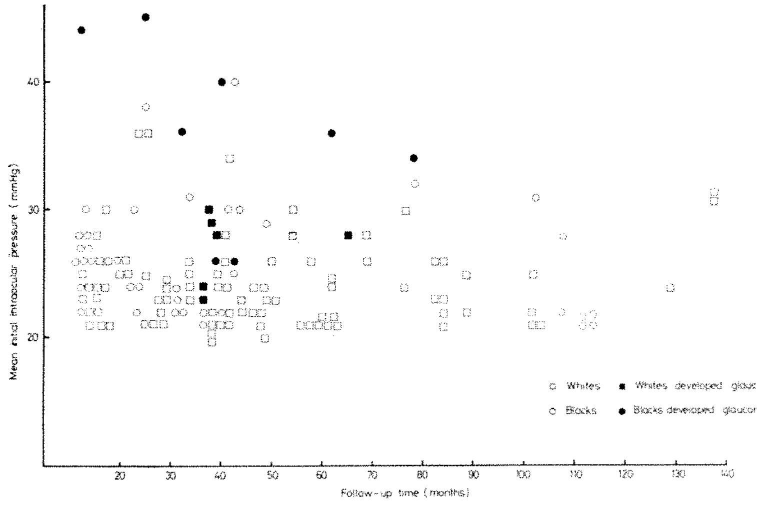


Fig. 2 *Mean initial IOP of patients with ocular hypertension in relation to follow-up time*

the highest incidence of glaucoma was found among patients with intraocular pressure of 31 mmHg or more (16·6% in the white ocular hypertensives and 50% of the blacks).

Discussion

The incidence of glaucoma developing from ocular hypertension is reported to be between 0·5% (Armaly, 1969) and 20% (Walker, 1974). These studies, however, do not specify whether the authors examined patients of different race groups and if any differences between these groups could be noted. In a recent report (Kitazawa *et al.*, 1977) a 9·3% incidence of glaucoma from ocular hypertension is reported in a group of patients from Japan.

Our study highlights several differences between black and white patients with ocular hypertension.

(1) The height of the mean intraocular pressure. In black patients 29 eyes (65·9%) presented with intraocular pressure higher than 26 mmHg as compared with 24 eyes (26%) among the white patients. In both groups the risk of glaucoma was directly related to the initial intraocular pressure

Table 1 *Relationship between the level of mean initial intraocular pressure (IOP) and the development of glaucoma from ocular hypertension in the 2 population groups*

IOP	*21 to 25 mmHg*			*26 to 30 mmHg*			*31 mmHg*			*Total*		
Patients	*Total*	*Glaucoma*	*%*	*Total*	*Glaucoma*	*%*	*Total*	*Glaucoma*	*%*	*Total*	*Glaucoma*	*%*
White	68	2	2·9	18	2	11·1	6	1	16·6	92	5	5·4
Black	15	—	—	17	2	11·7	12	6	50	44	8	18·1

(see Table 1), and this confirms other authors' findings that the IOP is the most reliable single factor in predicting future glaucoma from ocular hypertension (Armaly, 1969; Leydhecker, 1975). Thus black patients with ocular hypertension have a higher risk of developing glaucoma than white patients.

(2) In spite of the fact that in this study there were nearly twice as many white patients with ocular hypertension as blacks, 18·1% of the latter developed glaucoma compared with 5·4% in the whites.

(3) Age of presentation. The black patients with ocular hypertension were on average 12·6 years younger than their white counterparts. It is of interest that patients with primary open-angle glaucoma are also reported to be younger on average in the black population when compared with whites (Luntz, 1973b; Sarkies, 1953).

Among the white patients there is an increase in the number of patients with ocular hypertension with advancing age. This can be interpreted as a gradual increase in the intraocular pressure with age, an observation reported as far back as 1965 in the Oxford Glaucoma Survey (Luntz *et al.*, 1965). Nevertheless, in the white group with ocular hypertension, in spite of the increase in their number with age, the percentage of those developing glaucoma gradually decreases with every age decade, suggesting that the increase in the level of IOP noted with advancing age is a physiological rather than a pathological phenomenon.

We thank Mrs Ferelyth Douglas for her assistance with the technical illustrations.

References

Armaly, M. F. (1969). Ocular pressure and visual fields. *Archives of Ophthalmology*, **81**, 25–40.

Clarke, E. E. (1973). A comparative analysis of the age distribution and types of primary glaucoma among populations of African and Caucasian origin. *Annals of Ophthalmology*, **5**, 1055–1071.

David, R., Livingston, D., and Luntz, M. H. (1977). Ocular hypertension—A long-term follow-up of treated and untreated patients. *British Journal of Ophthalmology*, **61**, 668–674.

Kitazawa, Y., Horie, T., Aoki, S., Susuki, M., and Nishioka, K. (1977). Untreated ocular hypertension—A long term propspective study. *Archives of Ophthalmology*, **95**, 1180–1184.

Leydhecker, W. (1975). Tension tolerance. In *International Glaucoma Symposium, Albi*, 1974, pp. 193–204. Edited by R. Etienne. Diffusion Générale de Librarie: Marseille.

Luntz, M. H., Sevel, D., and Lloyd, J. P. F. (1965). The Oxford Glaucoma Survey—Statistical analysis of the results. *British Journal of Ophthalmology*, **49**, 128–136.

Luntz, M. H. (1972). Glaucoma and ocular hypertension. *South African Medical Journal*, **46**, 243–245.

Luntz, M. H. (1973a). Primary angle-closure glaucoma in urbanised South African caucasoid and negroid communities. *British Journal of Ophthalmology*, **57**, 445–456.

Luntz, M. H. (1973b). Primary open-angle glaucoma in urban negro and caucasian South African communities. *South African Archives of Ophthalmology*, **1**, 131–140.

Mann, I. (1972). *Causes and Prevention of Blindness*, pp. 40–43. Edited by I. C. Michaelson and E. R. Berman. Academic Press: London.

Monteiro de Gandt, D., and Maertens, K. (1973). Results of an enquiry on glaucoma simplex among black patients in the Republic of Zaire. *Annalles d' Oculistique*, **206**, 393–399.

Neumann, E., and Zauberman, H. (1965). Glaucoma survey in Liberia. *American Journal of Ophthalmology*, **59**, 8–12.

Sarkies, J. (1953). Primary glaucoma amongst Gold Coast Africans. *British Journal of Ophthalmology*, **37**, 615–620.

Walker, W. M. (1974). Ocular hypertension. Follow-up of 109 cases from 1963 to 1974. *Transactions of the Ophthalmological Societies of the United Kingdom*, **94**, 525–534.

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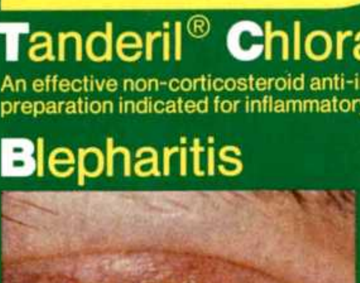

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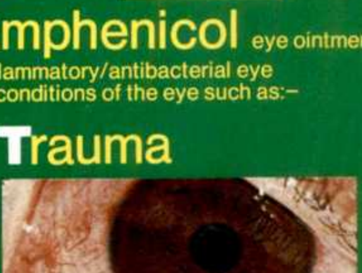

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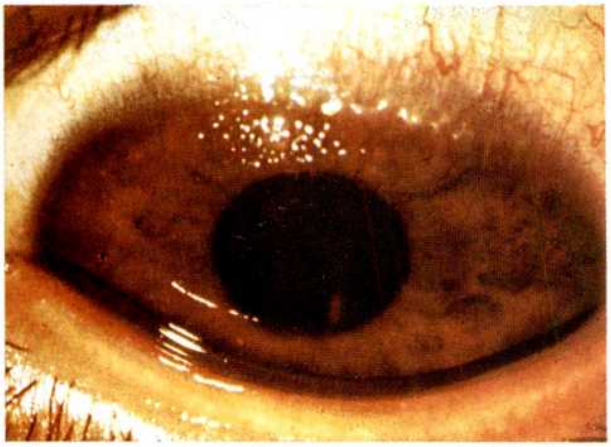
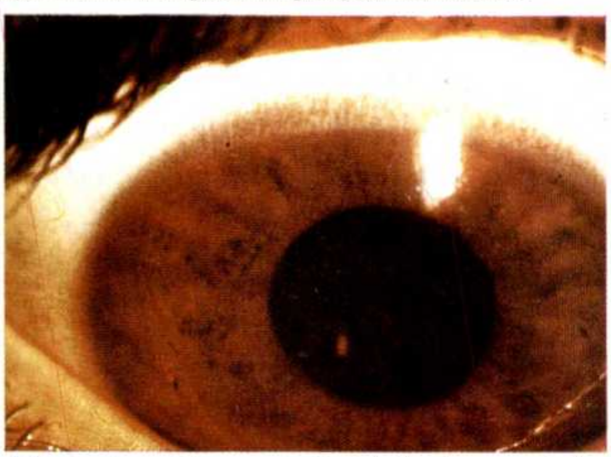


a. The superior limbus in a placebo treated eye of a patient suffering from vernal kerato-conjunctivitis, stained with fluorescein. Note the limbal hyperaemia and swelling and the irregularity of the corneal surface.



b. The opposite eye of the same patient treated with sodium cromoglycate eye drops. Before treatment, both eyes appeared similar.

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The effect of standardised submaximal work load on intraocular pressure

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SUMMARY A relatively small decrease in intraocular pressure secondary to submaximal work can be demonstrated when factors other than the work load itself are eliminated—diurnal variation, body position, and the effect of repeated examinations. A feedback mechanism that causes a return of IOP towards its normal value after work-induced decreases is postulated.

Decreases of intraocular pressure (IOP) related secondarily to physical exercise, have been reported (Leighton and Phillips, 1970; Marcus *et al.*, 1970a; Myers, 1974). It has been shown that this effect is inversely proportional to the work load (Lempter and Cooper, 1967; Kieler *et al.*, 1975). Other authors have found that IOP varies diurnally (Drance, 1960), changes with body position (Krieglestein and Langham, 1975), and the numerical value may be altered by the measuring technique itself (Duke-Elder, 1969).

The purpose of this study was to determine the effect of continuous and increasingly difficult periods of standardised submaximal work on intraocular pressure. The effect of all the previously mentioned factors were taken into account in analysing the data.

Subjects and methods

Eight healthy male volunteers aged 29 to 36 years (mean 31·4 years, SD 2·2 years) were studied. Their mean weight and height were 66·5 kg ±10·7 and 171·5 cm ±8·8, respectively. All subjects underwent an ophthalmological examination which included an ophthalmoscopic examination, anterior segment biomicroscopy, refractive error determination, and repeated applanation intraocular pressure determinations.

Six subjects were found to be emmetropic; one was myopic, −6·00 dioptres in both eyes; and one had −3·00 dioptres in the right eye and 5·50 dioptres in the left eye. No other ocular abnormality was found.

Before beginning this study none of the subjects had participated in a regular bicycle riding programme. Prediction of each subject's maximal oxygen uptake (VO_2 max) was assessed according to Astrand and Rodahl (1970). Mean VO_2 max was 41·8 ml/kg.min ± 6·2 and ranged from 36 to 50 ml/kg.min. The volunteers thus all fell into the range of individuals having average physical fitness.

Each person was tested 4 times by different exercise tests at 1-week intervals. Each session began at 9 a.m., 2 hours after breakfast. The laboratory temperature was 20°C. Four different test conditions were studied: *Condition A*, sitting upright on the bicycle ergometer for 1 hour; *condition B*, pedalling continuously at a rate of 50 cycles/min for 1 hour at a constant work load of 50 watts; *condition C*, an initial period of rest of 15 minutes followed at 9.15, 9.35, and 9.55 a.m. by a 5-minute period of pedalling at a rate of 50 cycles/min at light loads of 25, 50, and 75 watts, respectively (between active periods the subjects rested while seated on the ergometers); *condition D*, similar to condition *C*, but with moderate work loads of 100, 125, and 150 watts for the exercise period.

The intraocular pressure was measured in the last 30 seconds of the 19th, 39th, and 59th minutes under all conditions with a Drager applanation tonometer (Moller-Weder, West Germany) (Drager, 1967), under topical anaesthesia (benoxinate hydrochloride 0·2% and fluororescein sodium 0·25%). All measurements were performed by the same examiner, first on the right eye and then on the left eye.

Different orders of the conditions were used in

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Table 1 *Intraocular pressure for submaximal steady state work (mean and standard deviation, range, and significance of change compared to condition* A*). NS = not significant*

	Condition D	*Condition* C	*Condition* B	*Condition* A	*Time (h)*	
Mean ± SD	11·5 ± 1·7	15·0 ± 2·2	15·0 ± 3·1	17·3 ± 3·5	0920	Right
Range	10–15	10–19	10–18	12–24		eye
P <	0·001	0·001	0·005			
Mean ± SD	13·8 ± 4·2	13·6 ± 2·5	14·0 ± 4·5	15·5 ± 3·5	0940	
Range	8–22	10–17	8–18	10–20		
P <	NS	0·025	NS			
Mean ± SD	12·3 ± 2·6	13·7 ± 2·8	16·1 ± 3·2	15·8 ± 3·0	1000	
Range	9–16	11–18	11–21	10–19		
P <	0·025	0·05	NS			
Mean ± SD	13 ± 3·6	15·6 ± 3·0	16·1 ± 4·2	16·5 ± 4·2	0920	Left
Range	9–19	11–19	10–24	9–22		eye
P <	0·05	0·01	0·025			
Mean ± SD	11·6 ± 3·5	14·3 ± 4·0	15·7 ± 3·5	15·8 ± 4·2	0940	
Range	7–17	9–21	12–21	10–21		
P <	0·005	0·025	NS			
Mean ± SD	12·5 ± 3·5	12·1 ± 3·3	18·4 ± 2·7	13·7 ± 3·8	1000	
Range	6–17	8–16	15–23	9–20		
P <	0·05	0·025	0·010			

every 2 subjects (A, B, C, D; B, C, D, A; C, D, A, B; D, A, B, C). Data were evaluated by the paired Student *t* test when appropriate.

Results

Intraocular pressure (mean, standard deviation, and range) for the experimental conditions are listed in Table 1. The results of the first 40 minutes of continuous submaximal work load of 50 watts (condition *B*) show a slight decrease in IOP, but after 60 minutes of exercise the IOP rises to above the IOP measured at a similar period of rest (condition *A*). Stepwise increases in work load (conditions *C* and *D*) cause a decrease of IOP when compared to rest (condition *A*). There does not appear to be any correlation between further decrease in intraocular pressure and increasing work load ($P < 0{\cdot}05$).

Discussion

In the present study riding a bicycle ergometer was chosen for two reasons: the feasibility of examining the subjects' IOP during exercise, and because this form of activity is well accepted as a means for calibrated levels of physical exercise (Astrand and Rodahl, 1970).

Only a small decrease of IOP was found during submaximal work loads (conditions *B*, *C*, and *D*). For continuous pedalling at a work load of 50 watts (condition *B*) a fall was noted during the first 40 minutes, but a relative increase in IOP was noted at 60 minutes. No significant decreases of IOP were recorded with a stepwise increase of work load.

Previous investigations have reported more remarkable decreases of IOP during work (Leighton and Phillips, 1970; Marcus *et al.*, 1970a; Meyers, 1974) and larger drops of IOP with increases of work load (Lempter and Cooper, 1967; Kieler *et al.*, 1975). In some of these reports IOP changes were taken as the difference of measurements before and after work (Lempter and Cooper, 1967; Marcus *et al.*, 1971a; Meyers, 1974). This method does not account for either diurnal variation or the effect of repeated measurements. Diurnal changes can occur over as short a time as 20 minutes and may be as great as the changes noted during exercise (Henkind, 1973). In addition, repeated tonometric measurements may themselves lower the IOP (Stocker, 1958). In some of these studies the IOP was measured with the body in a different position from that in which the exercise was carried out (Lempter and Cooper, 1967; Leighton and Phillips, 1970; Kieler *et al.*, 1975). It is well known that a change in body position can also effect a change in IOP (Krieglestein and Langham, 1975). In some experiments the IOP was measured with a Schiotz tonometer (Lempter and Cooper, 1967; Kieler *et al.*, 1975), which is a less precise instrument than the applanation tonometer (Duke-Elder, 1969).

In the present study the change of IOP during work was the difference between the pressure measured at the end of steady state work and that for the same hour of the day and laboratory environment at rest. All measurements were made with an applanation tonometer with the subjects seated on the ergometer. By this method we attempted to exclude all the changes of IOP due to diurnal variation, body position, and repeated measurements with applanation tonometer. The attention paid to these factors in the present study explains the discrepancy between our results and the results of previous studies.

The physiological mechanisms responsible for the decrease of IOP at work are not clear (Kieler *et al.*, 1975). The decrease in IOP has been attributed to a decrease of blood pH and an increase in plasma osmolarity (Marcus *et al.*, 1970b). There may be a negative feedback mechanism causing a compensatory rise in IOP after the decrease induced by physical work. A similar feedback mechanism has been postulated to explain the increase of IOP that follows the initial pressure-lowering effects of ocular massage or hyperosmolar intravenous infusions (Robbins, 1971). In the continuous steady-state submaximal work (condition *B*) this feedback mechanism returned IOP towards its normal level after 40 minutes, with rebound seen as the IOP rises above its normal value at 60 minutes. Stepwise increases of work failed to show stepwise decreases of IOP due to the equalisation by the feedback mechanism.

It would appear from the data reported that two opposing mechanisms are affecting the intraocular pressure during a work load: (1) a fall secondary to physiological changes produced during exercise, and (2) a negative feedback attempting to stabilise the change. The result is that in the submaximal work range there is a small change in IOP.

References

Astrand, P. O., and Rodahl, K. (1970). Evaluation of physical work capacity on the basis of tests. In *Textbook of Work Physiology*, pp. 341–364. McGraw-Hill: New York.

Drager, J. (1967). Principle of clinical application of a probable applanation tonometer. *Investigative Ophthalmology*, **6**, 132–134.

Drance, S. M. (1960). The significance of the diurnal tension variations in normal and glaucomatous eyes. *Archives of Ophthalmology*, **64**, 494–501.

Duke-Elder, S. (1969). Diseases of the lens and vitreous glaucoma and hypotony. In *System of Ophthalmology*, Vol. II, pp. 455–456. Henry Kimpton: London.

Henkind, P., Leitman, M., and Weitzman, E. (1973). The diurnal curve in man: new observations. *Investigative Ophthalmology*, **12**, 705–707.

Kieler, R. A., Teraslinna, P., Rowe, D. G., and Jackson, J. (1975). Standardized aerobic and anaerobic exercise: differential effects on intraocular tension, blood pH, and lactate. *Investigative Ophthalmology*, **14**, 782–785.

Krieglestein, G. K., and Langham, M. E. (1975). Influence of body position on the intraocular pressure of normal and glaucomatous eyes. *Ophthalmologica*, **171**, 132–145.

Leighton, D. A., and Phillips, C. I. (1970). Effect of moderate exercise on the ocular tension. *British Journal of Ophthalmology*, **54**, 599–605.

Lempter, P., and Cooper, K. (1967). The effect of exercise on intraocular pressure. *American Journal of Ophthalmology*, **63**, 1673–1676.

Marcus, D. F., Krupin, T., Podos, S. M., and Becker, B. (1970a). The effect of exercise on intraocular pressure. I. Human beings. *Investigative Ophthalmology*, **9**, 749–752.

Marcus, D. F., Krupin, T., Podos, S. M., and Becker, B. (1970b). The effect of exercise on intraocular pressure. II. Rabbits. *Investigative Ophthalmology*, **9**, 753–757.

Meyers, K. J. (1974). The effect of aerobic exercise on intraocular pressure. *Investigative Ophthalmology*, **13**, 74–76.

Robbins, R. M., Obstbaum, S. A., and Galin, M. A. (1971). Intraocular pressure rebound. *British Journal of Ophthalmology*, **55**, 177–182.

Stocker, F. W. (1958). On changes in intraocular tension with application of tonometer. *American Journal of Ophthalmology*, **45**, 192–195.

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Effects of cigarette smoking on intraocular pressure and vision

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SUMMARY In a survey of 426 patients of Toronto ophthalmologists the correlations of reported smoking habits with (1) intraocular pressure and (2) visual acuity were examined. Average tonometer readings were closely similar in smokers, ex-smokers, and non-smokers, and multiple regression analysis showed similar age coefficients for the 3 categories. However, in women (but not in men) there was also a significant coefficient related to total cigarette exposure (puff-pack-years). It is suggested that this was due to recent smoking rather than a permanent effect on tonometer pressures, pointing the need to standardise this aspect of ocular pressure measurements. Visual acuity showed similar age coefficients in smokers, ex-smokers, and non-smokers, with no independent effect of exposure to cigarette smoke.

Previous papers from our laboratories have noted direct and 'passive' effects of cigarette smoke exposure on the eye (Sebben *et al.*, 1977; Basu *et al.*, 1977; Shephard *et al.*, 1978). Reactions include irritation, with an immediate disturbance of vision (Shephard *et al.*, 1978), lacrimation (Shephard *et al.*, 1978), and a shortening of the time to break up of the tear film (Basu *et al.*, 1977). In other contexts it has been widely accepted that exposure to irritant gases can cause open-angle glaucoma (Duke-Elder and Jay, 1969), with both acute and more long-term increases of intraocular pressure (Ballantyne and Swanston, 1977; Ballantyne *et al.*, 1977).

The situation with regard to cigarette smoking is less clearly established. Mehra *et al.* (1976) reported an acute rise of intraocular pressure >0·67 kPa* (5 mmHg) in 11·4% of normal subjects and 37·1% of patients with primary glaucoma; measurements were made within 5 minutes of the last puff on a cigarette, and normal pressures were restored within 15 to 30 minutes. On the other hand Bahna and Bjerkedal (1948) found no relationship between tonometer readings and reported smoking habits. Morgan and Drance (1975) also observed no association between smoking habits and the development of chronic open-angle glaucoma with associated optic disc change and field defects. However, in their study what was described as uncomplicated chronic glaucoma (ocular tension >2·79 kPa, 21 mmHg) was significantly associated with a high current cigarette consumption (more than 20 cigarettes a day).

The present report further examines the relationship of smoking habits to (1) intraocular pressures and (2) corrected vision.

Methods

The survey was conducted in co-operation with a number of ophthalmologists in Toronto who were measuring intraocular pressures as part of routine examinations of the visual system. A nurse attended the physicians' offices, soliciting volunteers, who completed a questionnaire on their smoking habits and visual reactions to cigarette smoke (Shephard *et al.*, 1978); they also agreed to release the data resulting from their ophthalmological examination.

A total of 426 adults over the age of 20 years were seen. After a standard clinical ophthalmological examination intraocular pressures were recorded by standard tonometric procedures, while visual acuity

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*The kilopascal is the unit of pressure now recommended by the International Committee on the standardisation of units.

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Table 1 *Reported current cigarette consumption of smokers, by age and sex*

Number of cigarettes per day	*Men*				*Women*			
	21–40 years (%)	*41–60 years* (%)	*>60 years* (%)	*All ages* (%)	*21–40 years* (%)	*41–60 years* (%)	*>60 years* (%)	*All ages* (%)
1–10	21·1	28·6	28·6	26·2	16·7	25·0	39·4	28·7
11–20	31·6	19·0	38·1	29·5	38·9	27·9	21·2	27·6
21–40	42·1	42·9	33·3	39·3	44·4	41·7	36·4	40·2
41 or more	5·3	9·5	—	4·9	—	5·6	3·0	3·4

Table 2 *Reported age of starting to smoke in relation to current consumption and to sex*

Number of cigarettes per day	*Men*					*Women*					
	Age of starting to smoke					*Age of starting to smoke*					
	1–12 years (%)	*13–20 years* (%)	*21–40 years* (%)	*41–60 years* (%)	*All ages* (%)	*1–12 years* (%)	*13–20 years* (%)	*21–40 years* (%)	*41–60 years* (%)	*61 or more years* (%)	*All ages* (%)
1–10	0	25·8	26·9	100·0	26·2	66·7	16·7	24·3	77·8	100·0	28·7
11–20	33·3	25·8	34·6	0	29·5	33·3	36·1	27·0	0	0	27·6
21–40	66·7	38·7	38·5	0	39·3	0	41·7	45·9	22·2	0	40·2
41 or more	0	9·7	0	0	4·9	0	5·6	2·7	0	0	3·4
Percentage of total sample	4·9	50·8	42·6	1·6	100·0	3·4	41·4	42·5	10·3	1·1	100·0

(corrected and uncorrected) was assessed by Snellen test charts.

Results

SUBJECTS AND SMOKING HABITS

Perhaps because the clinics were held during the daytime the sample included more women (269) than men (157); 89 subjects were aged 21 to 40 years, 167 were 41 to 60 years, and 170 were over the age of 60 years.

The proportion of current smokers (38·9% of the men, 32·3% of the women) was slightly lower than in previous Toronto (Shephard and LaBarre, 1978) and Provincial (Non-Medical Use of Drugs Directorate, 1976) samples, with 148 smokers (61 men, 87 women,) 96 ex-smokers (50 men, 46 women), and 182 non-smokers (46 men, 136 women). The pattern of current cigarette usage (Table 1) was much as expected; probably for financial reasons there were somewhat fewer heavy smokers (more than 20 cigarettes a day) in people aged over 60 years.

The largest number of subjects had begun to smoke between 13 and 20 years of age (Table 2), and this group seemed particularly vulnerable to a very high (more than 40 cigarettes a day) current consumption. Total cigarette exposure was calculated in terms of pack years and cigarette-puff years (puffs per cigarette × average daily consumption × 365 × years of smoking). The men tended to take more puffs per cigarette than the women (Table 3), average lifetime scores for the 2 groups being 2·45 and 1·46 million puffs respectively.

TONOMETRIC PRESSURES

Tonometric pressures conformed closely with previously reported data from other laboratories (Table 4). Values varied little with the reported cigarette consumption. If 2·8 kPa (21 mmHg) is taken as an upper limit of normality, this pressure was exceeded by 8 of 150 readings on smokers, 5 of 98 readings on ex-smokers, and 12 of 185 readings on non-smokers. However, in most of the smokers the excess pressure was small. Thus, if the limit of normality were extended to 2·1 kPa (22 mmHg), 2 of 150 smokers, 3 of 98 ex-smokers, and 10 of 185 non-smokers would have been regarded as abnormal.

When mean values were considered, there was a suggestion of an increment of pressure in the heavy smokers, particularly the women. This trend was supported when data were classified in terms of the number of puffs per cigarette (Table 5).

To test the significance of this tendency, multiple regression equations were established relating tonometer pressure, T (mean of right and left, mmHg), to age, A (years), and total cigarette exposure (pack years (PY) or puff-pack years (PPY); the significance of the 2 independent variables is shown in parenthesis:

Men and women

$T = 0{\cdot}076\,(A) - 0{\cdot}0013\,(PY) + 11{\cdot}46$ ($P<0{\cdot}005$, NS)
$T = 0{\cdot}069\,(A) - 0{\cdot}0024\,(PPY) + 11{\cdot}58$ ($P<0{\cdot}008$, NS)

Men

$T = 0{\cdot}141\,(A) - 0{\cdot}0352\,(PY) + 9{\cdot}61$ ($P<0{\cdot}009$, NS)
$T = 0{\cdot}128\,(A) - 0{\cdot}0108\,(PPY) + 10{\cdot}00$ ($P<0{\cdot}018$, NS)

Women

$T = 0{\cdot}071\,(A) + 0{\cdot}0268\,(PY) + 10{\cdot}83$ ($P<0{\cdot}031$, NS)
$T = 0{\cdot}075\,(A) + 0{\cdot}0106\,(PPY) + 10{\cdot}58$ ($P<0{\cdot}021$, $0{\cdot}040$)

The age effect was highly significant in all of these analyses, but after allowance for this variable the effects of cigarette exposure were relatively small, the one significant coefficient ($P<0{\cdot}040$) being for puff-pack years in the women.

The age coefficients for non-smokers (0·075±

Table 3 *Puffs per cigarette and total cigarette exposure (puffs per lifetime)*

Puffs per cigarette		*Percent of sample*	*Total cigarette exposure (million puffs per lifetime)*
Men	1–5	4·9	0·457
	6–10	42·6	1·984
	11–15	31·1	1·893
	16–20	19·7	4·632
	>20	1·7	5·183
Women	1–5	13·8	0·528
	6–10	47·1	0·909
	11–15	23·0	1·851
	16–20	14·9	3·112
	>20	1·2	6·027
Both sexes	1–5	10·1	0·514
	6–10	45·3	1·327
	11–15	26·4	1·871
	16–20	16·9	3·841
	>20	1·3	5·605

Table 5 *Intraocular pressure and puffs per cigarette. Mean ±SD*

	Intraocular pressure			
Puffs per cigarette	*Right eye*		*Left eye*	
	(mmHg)	*(kPa)*	*(mmHg)*	*(kPa)*
1–5 (n = 15)	14·7±4·2	1·96	15·5±3·9	2·06
6–10 (n = 64)	14·7±3·4	1·96	14·7±3·7	1·96
11–15 (n = 36)	15·0±4·4	2·00	15·4±4·3	2·05
16–20 (n = 23)	16·9±3·1	2·25	16·8±2·7	2·23
21 (n = 2)	17·3±1·8	2·30	17·3±1·8	2·30

Table 4 *Mean tonometer pressures and cigarette smoking. Mean ±SD*

	Male				*Female*				
	Right		*Left*		*Right*		*Left*		*Mean of right and left*
	(mmHg)	*(kPa)*	*(mmHg)*	*(kPa)*	*(mmHg)*	*(kPa)*	*(mmHg)*	*(kPa)*	*(mmHg)*
Non-smokers	16·1	2·14	15·1	2·01	15·5	2·06	15·3	2·03	15·4 (n = 182)
Ex-smokers	15·6	2·07	16·1	2·14	15·1	2·01	15·2	2·02	15·3 (n = 96)
Smokers									
1–10/day	16·0±3·9	2·13	16·3±4·5	2·17	14·9±3·5	1·98	15·2±3·3	2·02	15·5 (n = 69)
11–20/day	13·1±2·7	1·74	13·8±2·8	1·84	15·0±3·3	2·00	15·2±3·7	2·02	14·4 (n = 40)
21–40/day	16·9±4·7	2·25	16·2±4·1	2·15	15·2±4·5	2·02	15·2±4·6	2·02	16·0 (n = 25)
41 or more	16·0±4·2	2·13	15·5±3·5	2·06	18·3±3·8	2·43	18·8±4·5	2·50	17·2 (n = 4)

Table 6 *Visual acuity and cigarette consumption (% poor)**

	Uncorrected					*Corrected*				
	Male		*Female*		*All subjects mean of*	*Male*		*Female*		*All subjects mean of*
	Right	*Left*	*Right*	*Left*	*Right and left*	*Right*	*Left*	*Right*	*Left*	*Right and left*
Non-smokers	70·6	80·4	73·5	54·3	66·8	54·3	54·3	54·4	53·7	54·2 (n = 182)
Ex-smokers	65·2	63·0	80·0	80·0	76·0	50·0	50·0	40·0	42·0	43·3 (n = 96)
Smokers										
1–10/day	88·9	81·5	83·0	85·1	84·5	33·3	25·9	34·0	40·4	34·4 (n = 67)
11–20/day	93·8	75·0	56·0	56·0	67·1	31·3	37·5	52·0	56·0	46·4 (n = 40)
21–40/day	81·3	81·3	61·5	69·2	74·2	43·8	62·5	30·8	46·2	46·6 (n = 25)
>40	100·0	100·0	100·0	100·0	100·0	50·0	50·0	50·0	50·0	50·0 (n = 4)

*Poor is here defined as an acuity <10/20

Table 7 *Visual acuity and puffs per cigarette (% of sample in each category)*

Vision		*Puffs per cigarette*					
		1–5	*6–10*	*11–15*	*16–20*	*>21*	*All categories*
Uncorrected							
Right	Poor*	9·3	41·5	30·5	15·9	1·7	78·7 (n = 118)
	Normal	12·5	56·5	15·6	15·6	0	21·3 (n = 32)
Left	Poor	8·7	43·5	31·3	15·7	0·9	76·7 (n = 115)
	Normal	14·3	48·6	14·3	20·0	2·9	23·3 (n = 35)
Average right and left	Poor	9·0	42·5	30·9	16·3	1·4	77·7
	Normal	13·4	52·6	15·0	17·8	1·5	22·3
Corrected							
Right	Poor	12·1	44·8	20·7	20·7	1·7	38·7 (n = 58)
	Normal	8·7	44·6	31·5	14·1	1·1	61·3 (n = 92)
Left	Poor	12·1	50·0	16·7	18·2	3·0	44·0 (n = 66)
	Normal	8·3	40·5	35·7	15·5	0	56·0 (n = 84)
Average right and left	Poor	12·1	47·9	18·7	19·5	2·4	41·4
	Normal	8·5	42·6	33·6	14·8	0·6	58·7

*Poor is here defined as an acuity <10/20

0·027) and ex-smokers (0·115 ± 0·034) did not differ significantly from those for smokers.

VISUAL ACUITY

In view of the nature of our sample, most subjects had some impairment of visual acuity. Nevertheless, for purposes of statistical comparison it was possible to distinguish 2 categories—mild impairment (vision > 10/20) and 'poor' vision (acuity < 10/20). On this criterion the uncorrected vision of the smokers (78·1% of the sample with 'poor' vision) was possibly ($0{\cdot}2 > P > 0{\cdot}1$) a little poorer than that of the non-smokers (66·8% of the sample with 'poor' vision). The corrected vision was poorer in the heavy than the light smokers (Table 6) but was at least equally poor in the non-smokers.

The gradient of visual acuity with cigarette exposure was also seen when results were classified

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by puff frequency (Table 7). Those taking more than 10 puffs per cigarette included 48·5% of those with poor uncorrected vision but only 34·0% of those with normal vision. In terms of corrected vision the dividing line of 10 puffs per cigarette was less satisfactory, 40·0% of those with poor vision and 48·9% of those with normal vision exceeding this exposure. However, among those taking more than 15 puffs per cigarette were 21·3% of those with poor vision and only 15·3% of those with good vision.

Expressing the corrected visual acuity in digital terms (20/20=1·0)*, multiple regression equations were computed as follows:

Men and women

$V = -0{\cdot}0086\,(A) - 0{\cdot}006\,(PY) + 1{\cdot}25\ (P<0{\cdot}001, NS)$

$V = -0{\cdot}0089\,(A) - 0{\cdot}0001\,(PPY) + 1{\cdot}26\ (P<0{\cdot}001, NS)$

Men

$V = -0{\cdot}0100\,(A) - 0{\cdot}0005\,(PY) + 1{\cdot}34\ (P<0{\cdot}001, NS)$

$V = -0{\cdot}0115\,(A) - 0{\cdot}0001\,(PPY) + 1{\cdot}38\ (P<0{\cdot}001, NS)$

Women

$V = -0{\cdot}0069\,(A) - 0{\cdot}0001\,(PY) + 1{\cdot}14\ (P<0{\cdot}001, NS)$

$V = -0{\cdot}0069\,(A) - 0{\cdot}0001\,(PPY) + 1{\cdot}14\ (P<0{\cdot}001, NS)$

Again, the effect of age was highly significant, but after allowance for this variable the contribution of cigarette exposure was negligible, whether measured in pack years or puff-pack years. Age coefficients for ex-smokers (−0·0085±0·0020) and non-smokers (−0·0099±0·0013) were very similar to those for the smokers.

OVERT PATHOLOGY

Of the 148 smokers 1 had an overt cataract and 1 'vitreous floaters'. None of the 95 ex-smokers or 182 non-smokers had diagnoses related to glaucoma.

Discussion

TONOMETER PRESSURES

The present report supports the observations of Bahna and Bjerkedahl (1948) in showing almost identical mean intraocular pressures for non-smokers, ex-smokers, and smokers. However, the observations of Morgan and Drance (1975) are also substantiated in that (1) pressures are slightly higher in the small subgroup of subjects with a very high cigarette consumption, and (2) in women at least the multiple regression equation shows a significant effect of puff-pack years after allowance for the influence of age.

The average effect is of doubtful clinical significance (a pressure increment of about 0·27 kPa (2 mmHg)), although in the worst case (consumption of 2 packs per day for 40 years, with 20 puffs per cigarette), the multiple regression equation suggests that the rise of pressure could amount to 2·1 kPa (16 mmHg). The apparently larger effect on women is in keeping with their greater susceptibility to glaucoma (Armaly, 1965), and the correlation with puff-pack years but not pack years also suggests a true pharmacological effect. However, there was not a fixed period of abstinence from cigarettes either in the present study or in that of Morgan and Drance (1975), and the distribution of the increased pressures (6/8 < 2·9 kPa (22 mmHg)) supports the working hypothesis that we are seeing a transient response to recent smoking rather than a permanent elevation of pressure. This points the need for regulation of recent smoking when recording intraocular pressures. In the absence of such controls it is probably incorrect to regard as suffering from chronic uncomplicated glaucoma a patient who is a heavy smoker and has a pressure only a few millimetres of mercury above the average reading for non-smokers.

VISUAL ACUITY

The suggestion of a deterioration in visual acuity with an increase of cigarette consumption was not confirmed by our multiple regression analyses. We must conclude that neither the potential corneal irritation and lacrimation nor the threat of glaucoma has any effect on the ability to read standard clinical test type.

No great significance can be attached to the fact that the 1 case of overt cataract and the 1 case with vitreous floaters were both smokers. Since glaucoma develops only in about 1 patient in 200 over the age of 40 years (Armaly, 1965; Hollows and Graham, 1966; Bankes *et al.*, 1968), a much larger sample would be needed to compare the incidence of pathological changes between smokers and non-smokers.

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References

Armaly, M. F. (1965). On the distribution of applanation tension. *Archives of Ophthalmology*, 73, 11.

Bahna, S. L., and Bjerkedahl, T. (1948). Smoking and intraocular pressure. *American Journal of Ophthalmology*, 31, 1597.

Ballantyne, B., Gazzard, M. F., and Swanston, D. W. (1977). Applanation tonometry in ophthalmic toxicology. In *Current Approaches in Toxicology*. Edited by B. Ballantyne. J. Wright: Bristol.

Ballantyne, B., and Swanston, D. W. (1977). The scope and

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*Transformation of visual acuity into standard decimal format (e.g., 10/20 = 0·5) is a necessary preliminary to calculation of the multiple regression.

limitation of acute eye irritation tests. In *Current Approaches in toxicology*. Edited by B. Ballantyne. J. Wright: Bristol.

Banks, J. L. K., Perkins, E. S., Tsolakis, S., and Wright, J. E. (1968). Bedford glaucoma survey. *British Medical Journal*, **1**, 791.

Basu, J., Pimm, P., Shephard, R. J., and Silverman, F. (1978). The effect of cigarette smoke on the human tear film. *Canadian Journal of Ophthalmology*, **13**, 22.

Duke-Elder, S., and Jay, B. (1969). Diseases of the lens and vitreous: Glaucoma and hypotony. In *System of Ophthalmology*, Vol. II. Edited by Sir Stewart Duke-Elder. Henry Kimpton: London.

Hollows, F. C., and Graham, P. A. (1966). Intraocular pressure, glaucoma and glaucoma suspects in a defined population. *British Journal of Ophthalmology*, **50**, 570.

Mehra, K. S., Roy, P. N., and Khare, B. B. (1976). Tobacco smoking and glaucoma. *Annals of Ophthalmology*, **8**, 462.

Morgan, R. W., and Drance, S. M. (1975). Chronic open-angle glaucoma and ocular hypertension. *British Journal of Ophthalmology*, **59**, 211.

Non-Medical Use of Drugs Directorate (1976). Smoking habits of Canadians 1965–74. *Health and Welfare*. Ottawa, Ontario, Canada.

Sebben, J., Pimm, P., and Shephard, R. J. (1977). Cigarette smoke in enclosed public facilties. *Archives of Environmental Health*, March/April, p. 53.

Shephard, R. J., and LaBarre, R. (1978). Current attitudes towards smoking in Toronto. *Canadian Journal of Public Health*, **69**, 121.

Shephard, R. J., Ponsford, E., Basu, K., and LaBarre, R. (1978). Effects of cigarette smoke on the eyes and airways. *Canadian Journal of Public Health*. Submitted for publication.

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Effect of posture on the intraocular pressure of patients with retinal vein obstruction

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SUMMARY The effect of change of posture on the level of the intraocular pressure was studied in 22 patients who had suffered 'occlusion' of a central retinal vein, 14 patients with occlusion of a tributary of the central vein, and 23 normal subjects. The results showed a significant difference in behaviour between subjects in the control group and both groups of patients with retinal vein occlusions. In general it appears that the normal person maintains a relatively rigid control of ocular tension. The eyes are maintained at similar pressures which vary very little with change in posture. In contrast, the patient with a retinal vein occlusion (whether central or tributary) does not appear to have a similar degree of control. The eyes are not maintained at closely similar pressures, and each eye shows a change of pressure with change of posture which is considerably greater than that shown by the eyes of normal persons. The significance of these results is discussed with particular reference to the clinical association of retinal vein occlusion and chronic simple glaucoma, in which latter condition a similar lack of postural control of the intraocular pressure is found.

'Occlusion' of the central retinal vein or one of its tributaries is one of the commonest causes of sudden, serious and often permanent loss of vision seen in patients attending an eye clinic, and many of these patients are found to have a raised systemic arterial pressure. This condition must therefore be considered as a major complication of the retinopathy seen in these and other patients with hypertension of a comparable degree.

The cardinal feature of this retinopathy is an increase in the volume of the retinal veins. This is seen ophthalmoscopically as an increase in both their diameter and length, leading to the appearance of fat and tortuous vessels. Associated with this there is usually a variable degree of obscuration of the veins at the arteriovenous crossings due to an increase in the connective tissue sling which binds the artery and vein together at these points.

The appearance of the arteries is variable. They may be regular and give off a high reflex, or they may show irregularity of calibre and colour due to localised changes in their walls. When central vein occlusion supervenes, haemorrhages and exudates appear in all areas of the retina, and the veins appear dusky and grossly distended as though broken up into arched, ballooned segments which lie in the oedematous retina. When the vein involved is a tributary of the central vessel, a similar picture appears, with the difference that the changes are limited to the territory drained by the affected vessel and are virtually always situated distal to a point where it is crossed by an artery, fanning out to cover a wedge-shaped area with its apex at the arteriovenous crossing point.

The term venous 'occlusion' has come to replace venous 'thrombosis' since the studies of Verhoeff and others have shown that in the majority of these cases no true thrombus formation occurs (Verhoeff, 1907; Seitz, 1964). The term 'occlusion' may, however, also be a misnomer since retinal angiography with fluorescein has shown the affected vessel may be patent, when pictures are taken in the acute stage, as early as 1 day after the event (Smith *et al.*, 1964). Perhaps the term retinal vein 'obstruction' is more appropriate, since we do not know whether the lumen of the affected vessel must necessarily be obliterated, if only momentarily, before the retinal changes characteristic of this condition appear.

Despite the common occurrence of both central and tributary vein obstruction and their clinical association with systemic hypertension, we have as yet no knowledge of the sequence of events which provokes these lesions in certain patients. In the broadest of terms it seemed to us that some abnormal variation in the level of pressure in the retinal veins must be taking place. Two observations, made on

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patients referred to the medical clinic at the Western Ophthalmic Hospital following retinal vein obstruction, seemed to offer support to this view and prompted the studies which will be described in this paper.

The observations were as follows: (1) Most affected patients became aware of their visual loss in the morning, usually quite soon after they had got out of bed; (2) very many of these patients noticed a diurnal variation in their vision, saying that they saw less well in the morning than in the afternoon or evening.

An analysis of the known diurnal variation of intraocular tension in normal persons has shown that, while the pattern of variation is not constant, most people (65%) show maximum levels of tension at midnight or 5 a.m. (De Venecia and Davis, 1963.) Since our observations were noted in a similar proportion of patients it seemed possible that they might in some way be dependent on or at least related to these diurnal variations of pressure. Our hypothesis was that they reflected changes in the venous pressure occurring in the eye overnight and associated with leakage of fluid from capillaries, with resultant macular oedema. In the case of an established obstruction these events would be expected to cause a deterioration of vision in the morning with improvement as the day wears on and the sequence of pressure changes goes into reverse. By analogy a similar pattern of events could be supposed to be significant in the causation of an obstruction.

To test this hypothesis we decided to initiate a series of experiments designed to identify these supposed diurnal variations in the state of the retinal circulation. Our overall plan was to investigate a number of patients with various types of retinal vein obstruction by comparing morning and evening fluorescein angiograms of their retinae in the hope that we might identify such changes as alterations in venous calibre, capillary circulation, or degree of fluid exudation and be able to relate these to diurnal variations in visual acuity and systemic arterial and/or intraocular pressure.

During the course of preliminary experiments carried out on 6 of our patients with tributary vein obstructions we established that in all of them there was a diurnal variation in their intraocular tension, pressures recorded in the morning being consistently higher than those recorded in the evening in both eyes. The mean difference found in the affected eyes was 4·8 mmHg and in the non-affected eyes 5·9 mmHg.

Since we had been trying to mimic the normally occurring situation, morning readings had been taken while the patient was still in bed, in the supine position, whereas evening readings were taken with the patient in the sitting position, a Perkins hand-held applanation tonometer being used to make the measurements. This difference in posture could not, of course, be presumed as the sole cause of the different levels of pressure found, since the diurnal variation for any patient has been established using the Schiøtz tonometer, which involves the patient's being in the same position for all readings, that is, supine or semisupine. Nevertheless, we were interested to know how significant posture was, and so we decided to investigate the effect of relatively immediate changes of posture *per se* on levels of systemic arterial and intraocular pressure in certain of our patients and compare the results with those found in normal persons.

Patients and methods

SUBJECTS

We examined 3 groups of subjects, all of whom received a preliminary clinical examination: (1) 22 cases of central vein obstruction; (2) 14 cases of tributary vein obstruction; (3) 23 control subjects with no evidence of ocular disease.

The cases of central and tributary retinal vein obstruction were selected irrespective of age, sex, the supposed aetiology of the obstruction, or the presence of systemic hypertension. The duration of the obstruction varied among the subjects, and some were receiving coincident systemic therapy with drugs such as hypotensives, diuretics, steroids, etc., at the time of the investigation. One case of central vein obstruction was receiving local treatment (pilocarpine drops 1% twice daily) for chronic simple glaucoma which had developed after the obstruction.

AGE AND SEX

(1) *Central vein obstruction.* This group contained 12 male and 10 female patients. Their ages ranged from 26 years to 73 years, the mean age for the group being 59·4 years.

(2) *Tributary vein obstruction.* This group contained 8 male and 6 female patients. Their ages ranged from 52 years to 70 years, the mean age for the group being 60·8 years.

(3) *Control subjects.* This group contained 5 male and 18 female patients. Their ages ranged from 19 years to 70 years, the mean age for this group being 45·8 years.

METHOD

The subject was asked to sit quietly near one end of an examination couch for 15 minutes. The arterial pressure was then measured with a random recording sphygmomanometer, the average of 3

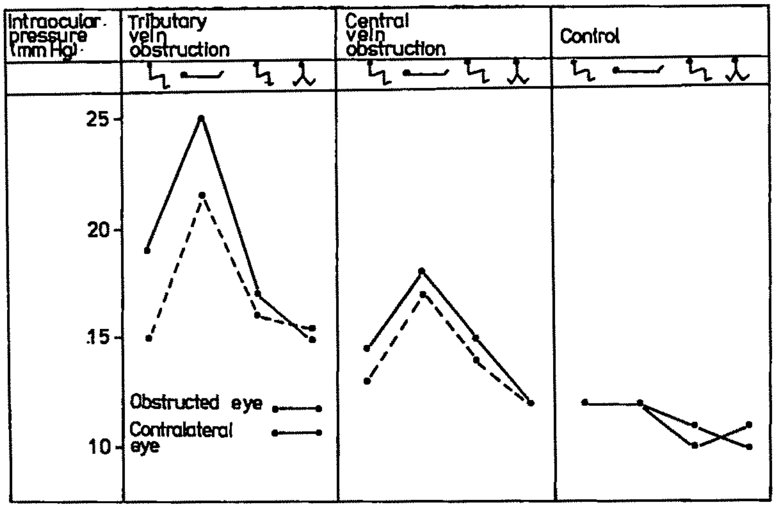

Fig. 1 *Typical postural pressure responses of 3 subjects in the age group 50 to 60 years*

readings being recorded. Oxybuprocaine 0·3% drops and fluorescein 0·125% were then instilled in both conjunctival sacs and the intraocular pressure measured with a Perkins hand-held applanation tonometer. The right eye was always examined first, 3 readings being taken, the mean of which was recorded. The subject was then asked to lie down (without getting up meanwhile), and after 15 minutes the arterial and intraocular pressures were measured and recorded as before. The subject was then asked to sit up, and after a further 15 minutes the readings were once more taken. Final measurements were taken with the patient in the standing position, these being recorded after he had been walking about at his normal pace for 15 minutes in the outpatient department.

We thus had 4 consecutive sets of readings for the various body positions, namely, sitting, supine, sitting, standing.

Results

INTRAOCULAR PRESSURE

An analysis of our results was made with respect to the following points: The relative levels of tensions in the 2 eyes, measured with the subject in the original sitting position; the difference in intraocular pressure existing between the 2 eyes of any subject, as measured in the original sitting position; the magnitude of any change in ocular pressure occurring when the subject went from the original sitting position to one in which he was lying down; the difference between the maximum and minimum intraocular pressures recorded in any eye, irrespective of the posture adopted (maximum amplitude).

The first measurements we considered were the levels of pressure in the obstructed and contralateral eye while the patient was in the original sitting position. We found that the pressure of the obstructed eye was lower than that of its colleague in 75% of those cases with tributary vein obstruction and in 68% of those cases with a central obstruction. The pressures were as follows (mean ± SD):

	Obstructed eye	*Contralateral eye*
Central vein obstruction	15·3 mm ± 2·7	17·0 mm ± 3·2
Tributary vein obstruction	14·7 mm ± 2·3	15·8 mm ± 2·3

In patients with central vein obstruction the levels of intraocular pressure in the obstructed eyes were significantly below those of their contralateral pairs (paired $t = 3{\cdot}29$, $2P < 0{\cdot}005$), whereas the pressures in the 2 eyes did not differ significantly in patients with tributary vein obstruction (paired $t = 1{\cdot}27$, $2P < 0{\cdot}3$). These findings are in agreement with those described by J. Foster Moore (1924) in his classic monograph.

We then considered the magnitude of any difference in pressure existing between the obstructed and contralateral eyes and compared this with that existing between the right and left eyes of the control subjects. Reference to Table 1 shows that the group of control subjects had a mean difference of 1·0 ± 1·0 mmHg, while the group of patients with tributary vein obstruction had a mean difference of 2·6 ± 1·9 mmHg, which is significantly greater (unpaired $t = 2{\cdot}9$, $2P < 0{\cdot}01$). The group of patients with central vein obstruction had a mean difference of 2·4 ± 2·1 mmHg, which is also significantly greater than that found in the control group (unpaired $t = 2{\cdot}86$, $2P < 0{\cdot}01$).

Change of position from sitting to lying also showed a further difference between patients and control subjects. The control subjects had a mean

Table 1 *Differences in intraocular pressure between subjects in different groups and between eyes within groups*

Groups of subjects	*No.*	*Intraocular pressure (mmHg)* *Mean difference right/left eyes*	*Mean rise on changing from sitting to lying* *Obstructed eye*	 *Fellow eye*	*Mean maximum amplitude* *Obstructed eye*	 *Fellow eye*
Tributary vein obstructions	14	2·6 ± 1·9	3·1 ± 2·3	2·1 ± 2·2	4·8 ± 2·5	4·6 ± 2·5
Central vein obstructions	22	2·4 ± 2·1	1·8 ± 2·4	2·6 ± 2·3	4·6 ± 1·9	5·1 ± 2·8
			Mean of 46 eyes		*Mean of 46 eyes*	
Control subjects	23	1·0 ± 1·0	0·6 ± 1·2		2·3 ± 1·6	

rise of 0·6 ± 1·2 mmHg for the 46 eyes in this group, which was compared separately with that found in each of the 2 eyes of patients in the other 2 groups. In the group of patients with tributary vein obstruction the mean rise was significantly greater in both the obstructed and contralateral eyes than that found in the control eyes. The mean rise in the obstructed eyes was 3·1 ± 2·3 mmHg (unpaired t = 3·85, 2P < 0·001) and in the contralateral eyes 2·1 ± 2·2 mmHg (unpaired t = 2·42, 2P < 0·02). In the group with central vein obstruction the mean rise was also significantly greater in both the obstructed and contralateral eyes than that found in the control eyes. The mean rise in the obstructed eyes was 1·8 ± 2·4 mmHg (unpaired t = 2·22, 2P < 0·05) and 2·6 ± 2·3 mmHg in the contralateral eyes (unpaired t = 3·45, 2P < 0·001).

The final quantity which we considered was the mean of the maximum amplitude. The control subjects showed a mean amplitude of 2·3 ± 1·6 mmHg for the 46 eyes which we compared separately with each of the 2 eyes of patients in the other groups. In the group of patients with tributary vein obstruction the mean maximum amplitude was significantly greater in both the obstructed and contralateral eyes than that found in the control eyes. The mean in the obstructed eyes was 4·8 ± 2·5 mmHg (unpaired t = 3·52, 2P < 0·001) and in the contralateral eyes, 4·6 ± 2·5 mmHg (unpaired t = 3·24, 2P < 0·005). In the group with central vein obstruction, the mean maximum amplitude was also significantly greater in both the obstructed and contralateral eyes than that found in the control eyes. The mean maximum amplitude was 4·6 ± 1·9 mmHg in the obstructed eyes (unpaired t = 4·89, 2P < 0·001) and 5·1 ± 2·8 mmHg in the contralateral eyes (unpaired t = 4·31, 2P < 0·001).

SYSTEMIC ARTERIAL PRESSURE

The arterial pressures (mean ± SD) recorded with the patient in the initial sitting position for the 3 groups of subjects were found to be as follows: (1) Patients with central vein obstruction, 149 (± 31)/89 (± 14). (2) Patients with tributary vein obstruction, 151 (±22)/98 (± 12). (3) Normal subjects, 117 (±18)/74 (±11).

Many of the patients in the first 2 groups, however, were receiving hypotensive drugs at the time of the study. The mean arterial pressures for these 2 groups as recorded in their outpatient notes before the commencement of hypotensive therapy were as follows: (1) Central vein obstruction, 157 (±34)/93 (±14). (2) Tributary vein obstruction, 169 (±20)/103 (±14).

It is seen from these figures that the patients who suffered a retinal vein obstruction had a higher mean systemic pressure than the persons in the control group and that those with a tributary obstruction had a somewhat higher mean pressure than those with a central obstruction at the time of the experiment. The level of hypertension even before treatment was, however, modest in the majority of patients, and some patients were normotensive.

We found no correlation between variations in systemic and intraocular pressure associated with the same change in posture (Hetland-Eriksen, 1966).

COINCIDENT THERAPY

At the time the experiments were carried out some of the patients with venous obstruction were receiving various systemic drugs including propranolol, methyldopa, clonidine, hydrochlorothiazide, Moduretic (amiloride and hydrochlorothiazide), bendrofluazide, cyclopenthazide, frusemide, spironolcatone, quinine sulphate, amitriptyline, allopurinol, nitrazepam, cholordiazepoxide, indomethacin, and prednisone. Fifteen out of 36 patients (41·6%) were receiving no treatment, while 21 patients (58·4%) were receiving 1 or more of the drugs listed above. We were unable to detect any significant difference in the pattern of the intraocular pressure response to change of posture between those patients receiving any of the drugs and those who were not.

DURATION OF OBSTRUCTION

The duration of the obstruction varied between 1 month and 5 years. The length of time between onset of obstruction and our measurements varied between 1 month and 3 years in tributary vein obstructions and between 6 weeks and 18 months in central vein obstructions. Although no obvious relationship is apparent between the duration of the obstructions and the pattern of the intraocular pressure response, we intend to repeat our observations at a suitable interval in order to assess any change in individual patients.

Discussion

From the results above it is seen that persons in our control group behave differently from the groups of patients with retinal vein obstruction. In general it appears that the normal subject maintains a relatively rigid control of ocular tension. The eyes are maintained at similar pressures which vary very little with change in posture. In contrast the patient with a retinal vein obstruction (whether central or tributary) does not appear to have a similar degree of control. The eyes are not maintained at closely similar pressures, and each eye shows a change of pressure with change of posture. Typically these eyes show a rise of about 2 to 3 mmHg associated with the change from sitting to lying (that is, approximately 4 to 6 times the change shown by normal eyes) and a maximum amplitude of pressure change between 4·5 and 5 mmHg (that is, more than twice that of normal eyes).

We have not been able so far to detect any variation in the intraocular pressure response dependent on levels of systemic pressure (or their variation with posture), the absence or presence of any therapy, or the duration of the obstruction, although we intend to study this further.

Two points of interest arise from these results. Firstly, the fact that both eyes—that is, obstructed and contralateral—show similar responses raises the question whether we have been measuring a quantity which is dependent on an abnormality which was present in both eyes before the obstruction occurred or is the result of the fact that 1 eye became the seat of an obstruction.

Secondly, various workers have shown that eyes with chronic simple glaucoma show a similar response to postural changes (Hetland-Ericksen, 1966; Anderson and Grant, 1973; Krieglstein and Langham, 1975; Langham, 1975). For the most part their studies have been concerned with the behaviour of eyes with open-angle, chronic simple glaucoma as compared with normal eyes, and they have reported a consistently different response in these 2 groups. The essential difference found has been related to the effect of changing the subject's position from sitting to lying. Normal persons have been recorded as showing lower rises of pressure following this manoeuvre. For example, Krieglstein and Langham (1975) studied 77 normal and 65 glaucomatous eyes and found an average rise of 2·9 mmHg in normal eyes as compared with 3·9 mmHg in glaucomatous eyes.

The similarity between the response shown by these glaucomatous patients and that found in our group of patients is interesting in view of the well-established clinical association between retinal vein obstruction and chronic simple glaucoma. The aetiological relationship that exists between these two conditions, however, remains obscure.

A number of clinical studies of the coincidence of the two conditions in 1 patient suggests that primary glaucoma has no special relationship with tributary vein obstruction but a highly significant one with central vein obstruction (Moore, 1924; Vannas and Tarkkanen, 1960; Bertelsen, 1961).

Thus Vannas and Tarkkanen (1960) found evidence of simple glaucoma as a pre-existing condition in only 10% of their patients with tributary vein obstructions, an incidence no greater than that found in a group of persons of comparable age selected from the general population, while they found an incidence of 42% in their cases presenting with a central obstruction. Other workers have found values for the coincidence of primary glaucoma and central vein obstruction as follows: 11% Baendstrup (1952); 43% Bertelsen (1961); 35% Raitta (1965).

Since these 2 groups of eyes—namely, glaucomatous and obstructed—appear to suffer from an inability to control their pressure in response to change of body position, our results might appear to suggest that eyes which develop chronic simple glaucoma and eyes which develop vein obstruction share a common defect which can produce either disease or both, depending on other as yet unknown factors. We have been impressed, however, with the similarity of the response in both tributary and central vein obstructions, although the mean rise of pressure on adoption of the supine position as well as the mean of the maximum amplitude was somewhat greater in the contralateral eye in those cases with a central obstruction. This may be of interest in view of the results of tonographic studies made by Vannas and Takkanen (1960) and Bertelsen (1961) on both eyes of patients with central vein obstruction. These studies showed that there was a greater facility of outflow in the obstructed as compared with the contralateral eyes.

Also of interest is the work of Inglima (1966), who performed postural tests on patients with unilateral simple glaucoma and found an abnormal response in the glaucomatous eyes but not in the contralateral normal eyes (Inglima, 1966). He carried out tonography on groups of normal and glaucomatous eyes and found a statistically significant relationship between facility of outflow and rise of intraocular pressure associated with the patient's change from a sitting to a supine position, that is, the lower the outflow the greater the rise of pressure. The postural effect was present in both eyes when both eyes suffered from an impaired facility of outflow and not otherwise.

Further studies are required to evaluate the significance of our findings for the understanding of the pathogenesis of retinal vein obstruction.

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References

Anderson, D. R., and Grant, W. M. (1973). The influence of position on intraocular pressure. *Investigative Ophthalmology*, **12**, 204–212.

Braendstrup, P. (1952). Centralvenethrombose—primaert glaucom. *Nordisk Medicin*, **48**, 1668–1669.

Bertelsen, T. I. (1961). The relationship between thrombosis in the retinal veins and primary glaucoma. *Acta Ophthalmologica*, **39**, 603–613.

De Venecia, G., and Davis, M. D. (1963). Diurnal variation of intraocular pressure in the normal eye. *Archives of Ophthalmology*, **69**, 752–759.

Hetland-Eriksen, J. (1966). On tonometry, 5. The pressure of glaucomatous eyes measured in the sitting and the lying positions by means of the Goldmann applanation tonometer. *Acta Ophthalmologica*, **44**, 515–521.

Inglima, R. (1966). Effect of patient position on applanometer readings. *Eye, Ear, Nose and Throat Monthly*, **45**, 64–69.

Krieglstein, G. K., and Langham, M. E. (1975). Influence of body position on the intraocular pressure of normal and glaucomatous eyes. *Ophthalmologica*, **171**, 135–145.

Langham, M. E. (1975). Vascular pathophysiology of the ocular postural response. A pneumotonometric study. *Transactions of the Ophthalmological Societies of the United Kingdom*, **95**, 281–287.

Moore, J. F. (1924). Retinal Venous Thrombosis. *British Journal of Ophthalmology*, Monograph Supplement, 2.

Raitta, C. (1965). Der Zentralvenen- und Netzhautvenenverschluss. *Acta Ophthalmologica*, Supplementum 83, 123.

Vannas, S., and Tarkkanen, A. (1960). Retinal vein occlusion and glaucoma. Tonographic study of the incidence of glaucoma and its prognistic significance. *British Journal of Ophthalmology*, **44**, 583–589.

Seitz, R. (1964). *The Retinal Vessels*, translated by F. S. Blodie. Mosby: St. Louis.

Smith, V., Paton, A., and Rubenstein, K. (1964). Arterial insufficiency in retinal vein occlusion. *Transactions of the Ophthalmological Societies of the United Kingdom*, **84**, 559–595.

Verhoeff, F. H. (1907). Obstruction of the central retinal vein. *Archives of Ophthalmology*, **36**, 1–36.

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Clearance of debris from the iris through the drainage angle of the rabbit's eye

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SUMMARY The fate of particulate material on entering the drainage angle of the rabbit's eye was investigated by transmission electron microscopy. The infiltrate was produced by photocoagulation of the iris. Initially it consisted of plasma, connective tissue and cellular debris, fibrin, and red blood cells. Later, free melanin granules, polymorphs, macrophages, and iris clump cells were all seen to enter the drainage system. Native meshwork cells were found to be active phagocytes and began to degrade various components of the infiltrate within 2 hours of the formation of the iris lesions. Corneal endothelial cells, the cells which cover the iris pillars, and the adventitial cells of the ciliary body were less active but were also phagocytic.

The mechanisms of disposal of particulate material through the primate drainage system have been studied by several investigators. It has been found that 2 mechanisms are of importance for the clearance of various forms of debris. Materials which can vary in size between horseradish peroxidase and red blood cells reach the endothelium of Schlemm's canal and enter the drainage vessels via transcellular pores (Segawa, 1971; Inomata *et al.*, 1972) through giant vacuoles (Feeney and Wissig, 1966; McRae and Sears, 1970; Tripathi, 1971, 1974; Inomata *et al.*, 1972) and to some extent by micropinosomes (Fine, 1964; Feeney and Wissig, 1966). If there is a fairly large particulate insult to the drainage system a second mechanism is evoked, that of phagocytosis by the native meshwork cells. Phagocytic activity by trabecular meshwork cells has been reported in the normal eye in various pathological situations and in experimental studies in which red blood cells (Shabo and Maxwell, 1972), colloidal gold and Indian ink (Rohen and Van der Zyphen, 1968), and bacteria and tapetum rods (Lee, 1971) have been injected into the anterior chamber.

Van der Zyphen (1977) has shown that the meshwork cells in rats have phagocytic properties, but there have been few other reports of phagocytic activity by meshwork cells in non-primates. The present investigation supplements and extends a preliminary report on the clearance through the rabbit outflow system of iris debris which was released after photocoagulation of the iris (Chisholm and Grierson, 1977).

In previous experimental studies the investigators studied the fate of a single injection of particulate material and its subsequent disposal (Rohen and Van der Zyphen, 1968; Shabo and Maxwell, 1972). The present study follows the progress of material which is continuously being released over a period of several days and, as such, is more comparable to pathological conditions.

Materials and methods

Twenty-four young adult Dutch rabbits were used in the present investigation. The animals were anaesthetised with veterinary pentobarbitone to a level at which the corneal reflex was absent. The iris in each animal was first constricted with 2% pilocarpine eye drops and 12 to 15 burns were made in the right iris of each animal. The photic burns were delivered by the Zeiss Oberkochun photocoagulator with the anterior chamber attachment. An instrument power setting which gave an output of 6 joules per second was chosen, and the duration of each burn was approximately 0·5 second.

The rabbits were killed by intracardiac air embolism under pentobarbitone anaesthesia from 2 hours to 90 days after photocoagulation. Both eyes were then enucleated and bisected into anterior and posterior halves under 3% glutaraldehyde in

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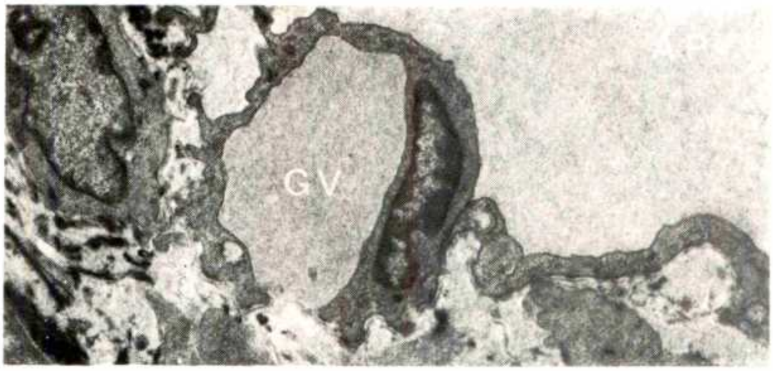

Fig. 1 *A giant vacuole (GV) in the endothelium of a vessel of the aqueous plexus (AP) 4 hours after photocoagulation. The vacuole contains plasma* (×7250)

cacodylate buffer. After primary fixation segments of limbal, corneal, and iridic tissues were removed and processed for electron microscopic examination.

Intraocular pressures were measured with a Draeger hand-held applanation tonometer before photocoagulation and then again before the eyes were enucleated. At no time after photocoagulation was intraocular pressure more than 3 mmHg higher in the test than in the corresponding control eye.

Results

LESIONS IN THE IRIS

The initial lesions appeared as discrete brown discolourations of the anterior surface of the iris. Thereafter the lesions began to enlarge, and blood, melanin, and other debris were present in the anterior chamber. At 10 days 1 or 2 of the burns had become through-and-through holes. By 90 days there was extensive necrosis of the iris, and much of the posterior surface was depigmented.

DRAINAGE ANGLE

Control tissue

The drainage angle of the control eyes conformed to the description outline by Tripathi (1974) for the normal rabbit outflow system. The angular region of the rabbit eye is distinguished by having a poorly developed ciliary muscle, a posterior extension of the anterior chamber angle called the ciliary cleft, and a plexus of aqueous collecting vessels called the angular aqueous plexus which corresponds to Schlemm's canal.

2 to 4 hours after photocoagulation

At 2 hours plasma filled the angle and most of the meshwork, but was not within the vessels of the acqueous plexus. There were a few red blood cells within the drainage tissues, and even at this early stage meshwork cells were engaged in the phacocytosis of red blood cells and plasma.

By 4 hours the infiltrate into the angular tissues was more complex and consisted of plasma, fibrin, disrupted cells, connective tissue debris, many red

Table 1 *The various phagocytic cells in the angular region, their diet, and their relative affinities for the various materials are indicated by these symbols: + present, ++ common, +++ abundant. The time period indicates when phagocytosis by the particular cell type was first identified*

	Hystiocytic macrophages	*Trabecular meshwork cells*	*Polymorphs*	*Adventitial cells of the ciliary body*	*Corneal endothelial cells*	*Cells which cover the iris pillars*
Red blood cells	+++	+++		+++		
Polymorphs	+++	++			+	
Melanin granules	+++	+++	++	++	++	+
Collagen debris	+++	+++	?	++		
Fibrin	+++	+++	+++	++		
Plasma	++	+++	+++	++		
	(4 hours)	(2 hours)	(1 day)	(2 days)	(2 days)	(7 days)

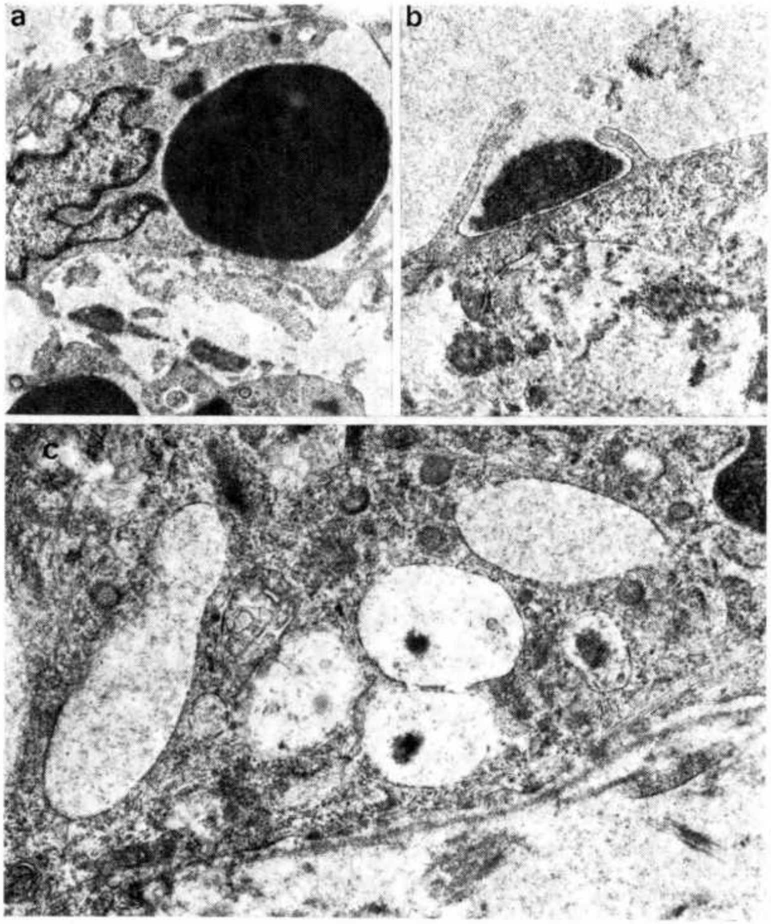

Fig. 2 *Meshwork cells in the outflow system 4 hours after photocoagulation. (a) A meshwork cell surrounding a red blood cell. (b) A clump of fibrin which is being enveloped by pseudopodia. (c) Vacuoles which contain plasma and fibrin within a meshwork cell* (a ×4200; b ×17 000; c ×25 000)

Table 2 *The various materials which entered the outflow system and their relative abundance at the appropriate time periods are indicated by these symbols:* + *present,* ++ *common,* +++ *abundant*

	Plasma	*RBCS*	*Collagen debris*	*Fibrin*	*Polymorphs*	*Melanin*	*Large iris cells*
2 hours	++	+	+				
4 hours	+++	+++	++	++			
1 day	+++	++	+++	+++	++	++	
2 days	+++	++	+++	+++	+++	+++	
4 days	+?	++	++		+++	+++	
7 days		+	+?		+	++	+
10 days		+			+?	+	++
14 days		+				+	+++
18 days		+					+++
30 days		+					+++
90 days							+

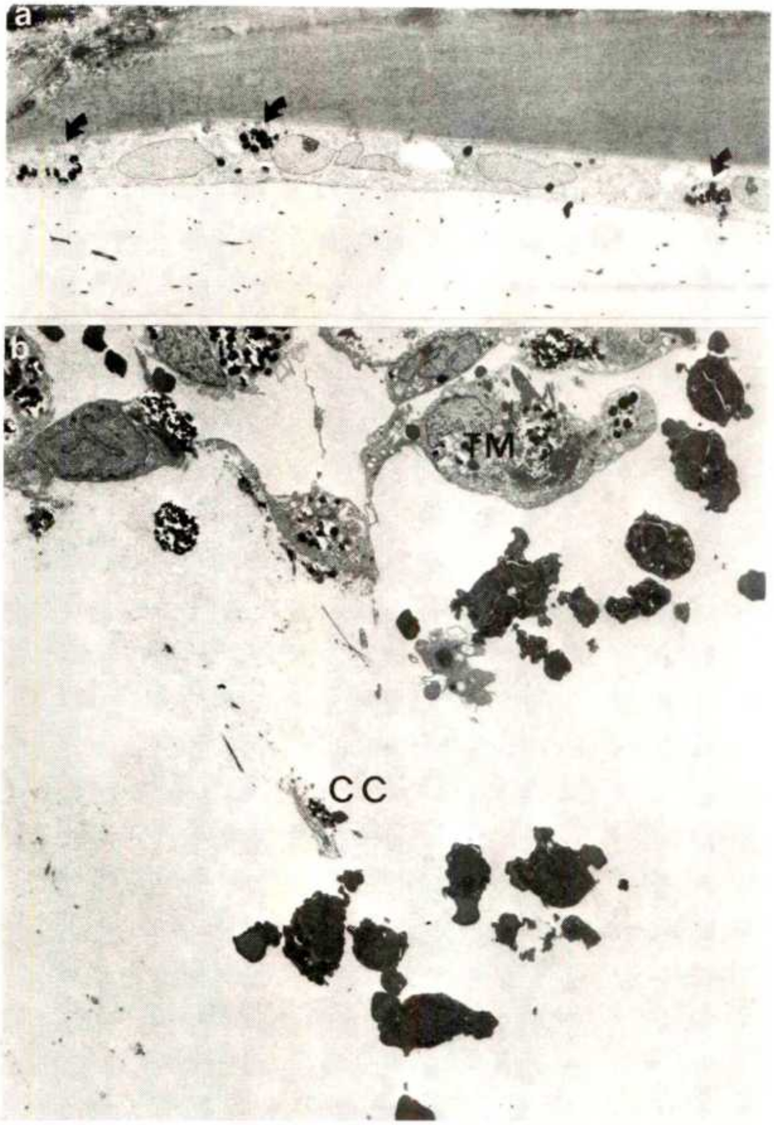

Fig. 3 *The angular region 2 days after photocoagulation. (a) Corneal endothelial cells close to the ciliary cleft, which contain melanin granules (arrows). (b) Beneath the trabecular meshwork (TM) the ciliary cleft (CC) contains large numbers of polymorphs* (a × 1600; b × 1520)

cells, and an occasional macrophage. All the various materials were observed within the giant vacuoles of the endothelium lining the aqueous collecting vessels and had penetrated into the lumina of these vessels (Fig. 1).

Not only did the infiltrate pass through the conventional drainage system but there was lateral passage of the various materials into the ciliary body via the interstitial spaces. Presumably the infiltrate was moving towards the suprachoroid by the so-called uveoscleral drainage route.

In the absence of substantial numbers of macrophages from outside the drainage area the native meshwork cells were the predominant phagocytes in the tissue (Fig. 2 and Table 1).

1 to 4 days after photocoagulation

On day 1 the infiltrate contained 2 additional components, polymorphonuclear leucocytes and melanin granules (Table 2). Many more meshwork cells were now involved in phagocytosis, but they were no longer exclusively phagocytes. Large numbers of histiocytic macrophages were present within the drainage system. The histiocytic macrophages were engulfing a similar range of materials to that taken by the native meshwork cells. The polymorphs

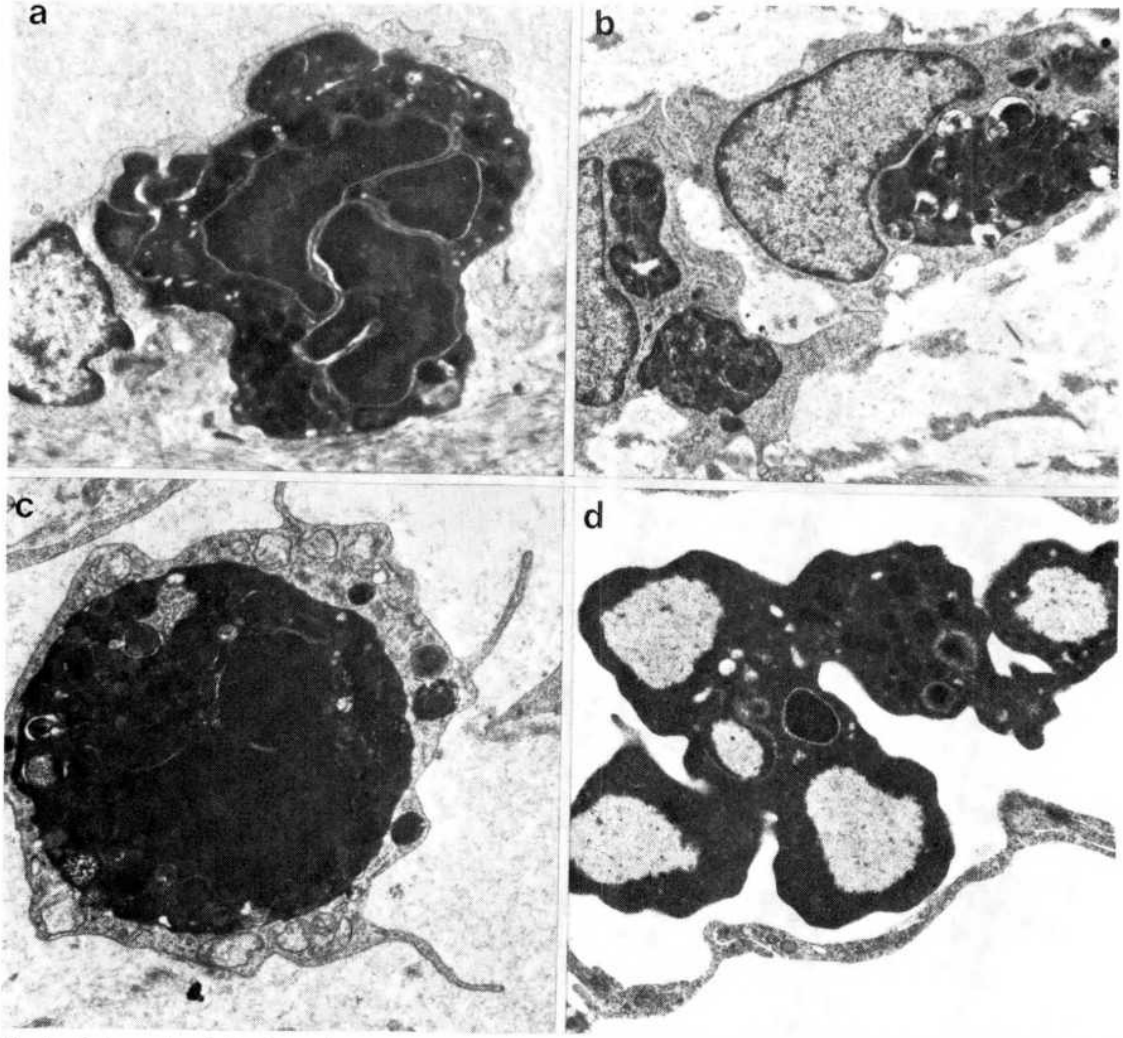

Fig. 4 *Polymorphs within the outflow system. (a) A polymorph partially within the lumen of a giant vacuole 2 days after photocoagulation. (b) Polymorph debris within a meshwork cell 4 days after photocoagulation. (c) A fragment of a polymorph which is contained within a macrophage 2 days after photocoagulation. (d) A degenerate polymorph 4 days after photocoagulation* (a × 7500; b × 11 700; c × 12 500; d × 13 300)

were also active phagocytes, but their diet was restricted to fibrin and plasma.

On day 2 the corneal endothelial cells began to incorporate melanin granules (Fig. 3) and the ciliary adventitial cells had started to ingest plasma, fibrin, and other debris (Table 1). Polymorphs had become more frequent; some were engulfing melanin while others were beginning to degenerate. The more vigorous phagocytic cells had in turn begun to ingest the degenerating polymorphs (Fig. 4).

By the second day some of the meshwork cells had become 'activated', which was a process whereby a meshwork cell became detached from the connective tissue of a trabecula and lost its normal association with neighbouring meshwork cells to become fully mobile. The activated meshwork cell was called an endothelial macrophage to distinguish it from the histiocytic or non-native macrophage.

Though it was often difficult to distinguish between endothelial and histiocytic macrophages the former usually had darker cytoplasm and more rough endoplasmic reticulum, and their nuclei were often heavily infolded. The most obvious difference was that histiocytic macrophages had many filopodia or

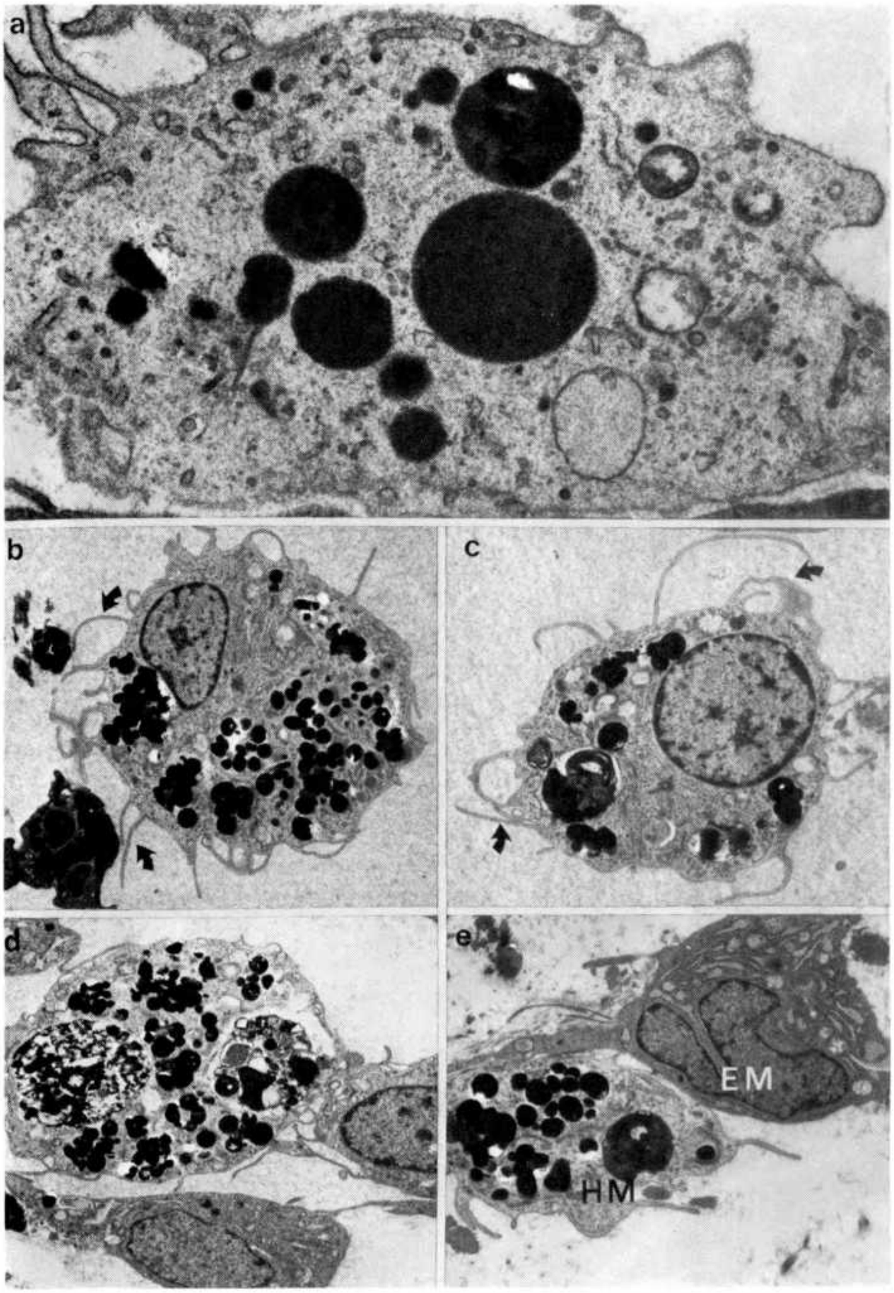

Fig. 5 *Histiocytic macrophages within the outflow system 2 days after photocoagulation. (a) A histiocytic macrophage which contains fragments of haematogenous material. (b) and (c) Histiocytic macrophages with prominent filopodia (arrows) which have ingested melanin granules. (d) A pale staining histiocytic macrophage which contains large secondary lysosomal complexes. (e) A histiocytic macrophage (HM) can be compared with an endothelial macrophage (EM)* (a ×16 800; b ×2800; c ×2800; d ×3000; e ×3850)

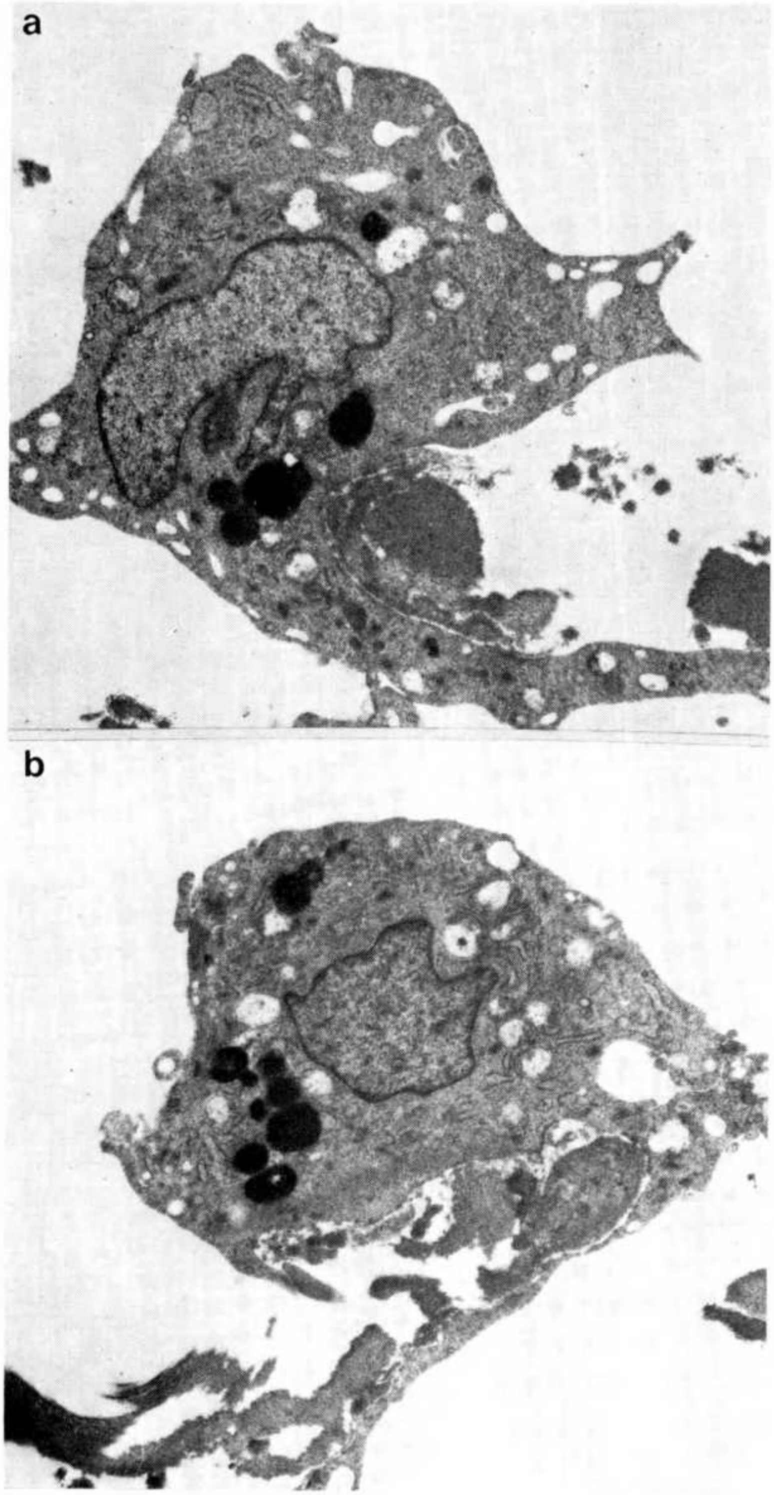

Fig. 6 *Meshwork cells in the process of detachment and 'activation' 7 days after photocoagulation. In both (a) and (b) the cells appear to be becoming detached and free moving* (×10 300)

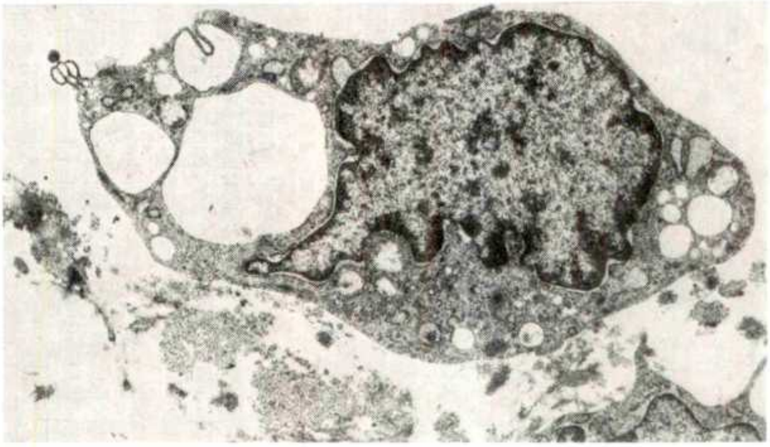

Fig. 7 *A meshwork cell 7 days after photocoagulation. The cell is no longer associated with other meshwork cells and is therefore considered to be 'free' and 'activated'. The meshwork cell contains numerous large electron-lucent vesicles, which indicates that this macrophage has been heavily committed to the degradation of plasma and fibrin* (×8600)

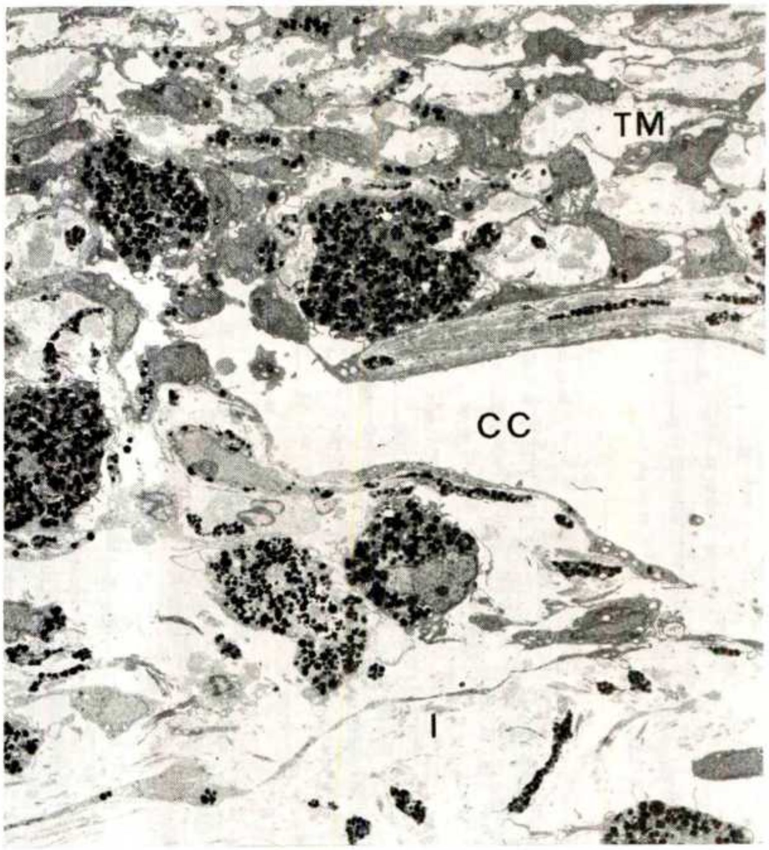

Fig. 8 *Large rounded pigmented iris cells in the iris root (I) and the trabecular meshwork (TM) 10 days after photocoagulation. The ciliary cleft (CC) is now cleared of most of the fine particulate debris; however, the trabecular meshwork cells contain numerous melanin granules* (×2100)

cytoplasmic processes which projected from the cell surface, whereas the endothelial macrophages and trabecular meshwork cells did not have these structures (Figs. 4*c*, 5, 6, and 7). Four days after photocoagulation the polymorphs were extremely degenerate and had pyknotic nuclei, patchy areas of cytoplasmic lucency, and bizarre outlines (Fig. 4*d*). These cells were rapidly being lost from the system either through the drainage channels or by vigorous phagocytosis (Fig. 4). The route taken by red blood cells, polymorphs, histiocytic macrophages, and endothelial macrophages into the aqueous plexuses

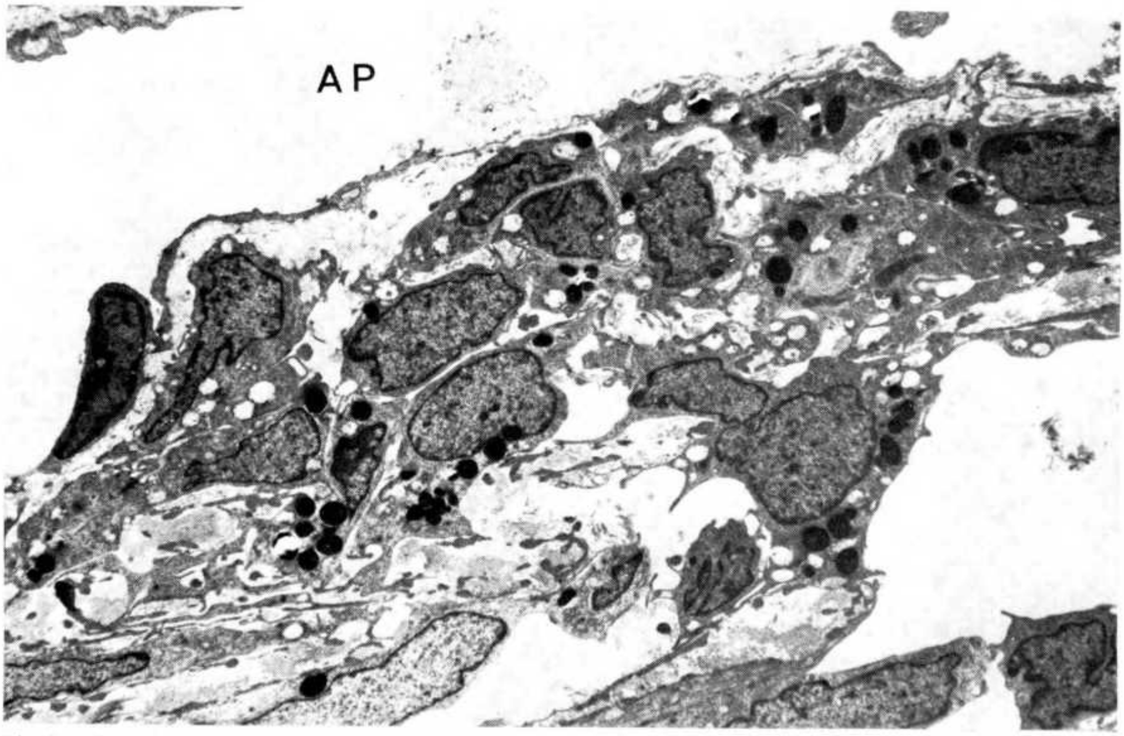

Fig. 9 *The trabecular tissues close to a vessel of the angular aqueous plexus (AP) 30 days after photocoagulation of the iris. The endothelium which limits the vessel is discontinuous (arrows)* (× 5000)

was either via giant vacuoles or through the narrower attenuated portions of the endothelium, but the particulate debris used only the vacuolar pathway (Table 3).

7 to 90 days after photocoagulation

Seven days after photocoagulation large pigmented iris cells with diameters in excess of 15 μm had arrived in the drainage system. It appeared likely that they were mobilised iris stromal clump cells and detached posterior iris epithelial cells (Fig. 8 and Table 2). There was no evidence to indicate that these large pigmented cells were phagocytic when present in the drainage system. By day 18 the pigmented iris cells had penetrated deeply into the trabecular meshwork and had caused considerable structural damage during their passage. The pigmented cells were too large to pass through the normal trans-endothelial pore system of the aqueous plexuses, and as a result of their accumulation they impinged on the endothelium lining the vessels, which resulted in cellular separation.

The damage to the meshwork and the aqueous plexuses was particularly evident on day 30 (Fig. 9), which was the period when the accumulation of pigmented iris cells was greatest. At this stage the trabecular meshwork was extremely loose and disorganised, partly because of the damage caused by the large iris cells and partly because of the activation of so many meshwork cells into mobile endothelial macrophages.

Only a few pigmented iris cells remained 90 days after photocoagulation, and the endothelium of the angular aqueous plexus had re-formed into an intact monolayer. The outflow system had to some extent

Table 3 *The exit route for the passage of the infiltrate through the endothelium which surrounds the vessels of the aqueous plexus*

Exit route into the vessels of the aqueous plexus	*Particulate materials in outflow system*
Giant vacuoles	Plasma, fibrin, connective tissue debris, cellular debris, and free melanin granules
Giant vacuoles and transcellular channels	Red blood cells, polymorphonuclear leucocytes, histiocytic macrophages, and endothelial macrophages
Ruptures in the vessel endothelial monolayer	Large pigmented iris cells

returned to normal except that it was deficient in native meshwork cells.

Discussion

The fate of particulate material which enters the rabbit drainage system is either *(a)* to pass through the trabecular meshwork and into the vessels of the angular aqueous plexus, or *(b)* to move into the ciliary body via the interstitial spaces, or *(c)* to be engulfed by phagocytic cells.

Giant vacuoles serve as the main route by which aqueous is transferred across the endothelium surrounding the vessels of the angular aqueous plexus (Tripathi, 1974). Therefore the mechanism of fluid passage is similar to that into Schlemm's canal in primates (Holmberg, 1965; Kayes, 1967; Tripathi, 1968, 1971; Inomata *et al.*, 1972; Grierson and Lee, 1974, 1975). In the present investigation we have shown that giant vacuoles not only serve as a drainage pathway for aqueous humour but allow the egress of particulate material and cells from the meshwork into the lumina of the vessels. Mobile flexible cells like macrophages, polymorphs, and even red blood cells have a second option, and that is to pass through a transcellular opening which does not involve the formation of a giant vacuole. The so-called non-vacuolar transcellular channels have been described in the endothelium on the trabecular aspect of Schlemm's canal in the primate (Segawa, 1971; Inomata *et al.*, Smelser, 1972; Grierson and Lee, 1975). Thus the system of vacuolar and non-vacuolar channels can be considered both as a drainage pathway and as a safety mechanism. By allowing the passage of particulate material from the spaces of the endothelial meshwork the dual hazards of abnormal elevation of intraocular pressure and loss of integrity of the endothelial monolayer can be avoided. Seven days after photocoagulation large pigmented iris cells began to enter the outflow system. The large pigmented iris cells could not pass through the transendothelial channels. Thus the safety mechanism was ineffectual, and the endothelial monolayer was disrupted by the build-up of these large cells in the endothelial meshwork. Similar large pigmented iris cells have been described in the outflow system of a patient with pigment dispersion phenomena (Iwamoto *et al.*, 1971).

The phagocytic capability of the native trabecular meshwork cells in the rabbit outflow system appears to be well developed. These cells can engulf and degrade a great variety of material from fibrin and plasma to polymorphs and red blood cells. Phagocytosis can be evoked in a remarkably short time, so that by 2 hours after photocoagulation some meshwork cells had taken in red cells and plasma. The native meshwork cells are not the only local phagocytes in the drainage angle, since corneal endothelial cells, the cells which cover the iris pillars, and the adventitial cells of the ciliary body also could be stimulated, but only after prolonged exposure to the infiltrate. The phagocytic behaviour of the rabbit trabecular meshwork cells is very similar to that described in the monkey (Rohen and Van der Zyphen, 1967) and in man (Grierson and Lee, 1973). The cells become activated after their phagocytic burden has reached a critical level and lose contact with their neighbours to become wandering histiocytes.

The ability of native meshwork cells to become active phagocytes is of some importance, and malfunction of this phagocytic process has been proposed as a possible contributory factor to the development of primary open-angle glaucoma (Bill, 1975). Certainly in many of the conditions which are classified as secondary open-angle glaucoma such as haemolytic glaucoma (Yamashita and Rosen, 1965), pigmentary glaucoma (Iwamoto *et al.*, 1971), and pseudoexfoliation glaucoma (Ringvold and Vegge, 1971) meshwork cells actively ingest components of the various infiltrates. Therefore it can be assumed that, if the infiltrates are responsible for the pathological elevation of the intraocular pressure, they must invade the drainage tissues in such quantities that neither the vacuolar drainage channels nor the filtering capabilities of the meshwork cells can cope with the influx.

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References

Bill, A. (1975). The drainage of aqueous humour. *Investigative Ophthalmology*, **14**, 1–3.

Chisholm, I., and Grierson, I. (1977). Particulate phagocytosis by trabecular meshwork endothelium. *Canadian Journal of Ophthalmology*, **12**, 293–299.

Feeney, M. L., and Wissig, S. (1966). Outflow studies using an electron dense tracer. *Transactions of the American Academy of Ophthalmology and Otolaryngology*, **70**, 791–798.

Fine, B. S. (1964). Observations on the drainage angle in man and monkey. *Investigative Ophthalmology*, **3**, 609–646.

Grierson, I., and Lee, W. R. (1973). Erythrocyte phagocytosis in the human trabecular meshwork. *British Journal of Ophthalmology*, **57**, 400–415.

Grierson, I., and Lee, W. R. (1974). Changes in the monkey outflow apparatus at graded levels of intraocular pressure:

a qualitative analysis by light microscopy and scanning electron microscopy. *Experimental Eye Research,* **19,** 21–33.

Grierson, I., and Lee, W. R. (1975). Pressure induced changes in the ultrastructure of the endothelium lining Schlemm's canal. *American Journal of Ophthalmology,* **80,** 863–884.

Holmberg, A. S. (1965). Schlemm's canal and the trabecula meshwork. An electron microscopic study of the normal structure in man and monkey (*Cercopithecus ethiops*). *Documenta Ophthalmologica,* **19,** 339–373.

Inomata, H., Bill, A., and Smelser, G. K. (1972). Aqueous humour pathways through the trabecular meshwork and into Schlemm's canal in the cynomolgus monkey (*Macaca irus*). An electron microscopic study. *American Journal of Ophthalmology,* **73,** 760–789.

Iwamoto, T., Witmer, R., and Landolt, E. (1971). Light and electron microscopy in absolute glaucoma with pigment dispersion phenomena and contusion angle deformity. *American Journal of Ophthalmology,* **72,** 420–434.

Kayes, J. (1967). Pore structure of inner wall of Schlemm's canal. *Investigative Ophthalmology,* **6,** 381–393.

Lee, W. R. (1971). The study of the passage of particles through the endothelium of the outflow apparatus of the monkey eye by scanning and transmission electron microscopy. *Transactions of the Ophthalmological Societies of the United Kingdom,* **91,** 687–705.

McRae, D., and Sears, M. L. (1970). Peroxidase passage through the outflow channels of human and rhesus eyes. *Experimental Eye Research,* **10,** 15–18.

Ringvold, A., and Vegge, T. (1971). Electron microscopy of the trabecular meshwork in eyes with exfoliation syndrome (Pseudo-exfoliation of the lens capsule). *Virchows Archiv für pathologische Anatomie und Physiologie und für klinische Medizin,* **353,** 110–127.

Rohen, J., and Zyphen, E. (1968). The phagocytic activity of the trabecular meshwork endothelium. *Albrecht von Graefes Archiv für klinische und experimentelle Ophthalmologie,* **175,** 143–160.

Segawa, K. (1971). Pores of the trabecular wall of Schlemm's canal: Ferritin perfusion in enucleated human eyes. *Japanese Journal of Ophthalmology,* **15,** 1–8.

Shabo, A. L., and Maxwell, D. S. (1972). Observations on the fate of blood in the anterior chamber. A light and electron microscopic study of the monkey tabecular meshwork. *American Journal of Ophthalmology,* **73,** 25–36.

Tripathi, R. C. (1968). Ultrastructure of Schlemm's canal in relation to aqueous outflow. *Experimental Eye Research,* **7,** 335–341.

Tripathi, R. C. (1971). Mechanism of aqueous outflow across the trabecular wall of Schlemm's canal. *Experimental Eye Research,* **11,** 116–121.

Tripathi, R. C. (1974). Comparative physiology and anatomy of the aqueous outflow pathway. In *The Eye,* vol. 5, pp. 163–356. Edited by H. Davson. Academic Press: London.

Van der Zyphen, E. (1977). Experimental morphological study on structure and function of the filtration angle of the rat eye. *Ophthalmologica,* **174,** 285–298.

Yamashita, T., and Rosen, D. A. (1965). Electron microscopic study of trabecular meshwork in clinical and experimental glaucoma with anterior chamber hemorrhage. *American Journal of Ophthalmology,* **60,** 427–434.

British Journal of Ophthalmology, 1978, **62**, 705–708

The perimeter as a monitor of glaucomatous changes

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SUMMARY A small group of glaucoma patients with scotomata were compared with normal coevals. Plots were obtained of the error of each measurement as a function of retinal illumination. A statistical analysis shows the limitations of perimetry as a monitor of the progress of glaucoma. The significance of the data is discussed.

The primary concern of both the glaucomatous patient and his ophthalmologist is that the treatment prescribed should control the condition. A reduction in the intraocular pressure (IOP) to a so-called 'normal' level is only an indication of control, since it has been found that individuals vary in their tolerance to different levels of IOP (Armaly, 1969). It therefore becomes increasingly important to find the most accurate method of determining changes in the visual field.

Sloan (1939) used a modified Ferree-Rand perimeter and introduced static perimetry as a clinical method of examining the visual field. The technique was further advanced by Goldmann (1945) and later by Harms (1950) and Harms and Aulhorn (1959). It is found that static perimetry gives a much greater reproducibility of results (Drance *et al.*, 1967) than does kinetic perimetry. Accordingly we set out to discover within what limits this reproducibility occurs (*cf.* Verriest and Israel, 1965).

Method

The 10 patients in this study had a visual acuity better than 6/12 (0·5), good fixation, low refractive errors, and IOPs not greater than 22 mmHg on medication. In order to minimise fatigue only 1 scotomatous eye of each patient was tested. Three normal controls of the same age group were also tested. Each patient underwent 4 sets of tests on the Tübingen Oculus within a few days of one another. The pupil size was recorded.

The IOP of each patient was measured before and after each test. The eye was dilated with phenylephedrine 10% and cyclopentolate 1% for 30 minutes. The appropriate reading correction was then placed in front of the dilated eye and the patient allowed to adapt to the background illumination of 10 asb for 5 minutes (Greve, 1973, p. 30).

A supraliminal 10′ red fixation target was used. The test target was similar in size but white, and the exposure time kept short at 1/10 s (Greve, 1973, p. 86) to eliminate photic waste and vitiating effects of eye movements. The thresholds were measured infra- to supraliminally starting 1° from the fovea and going out to 30° in the following way: first the fovea, then the upper nasal, upper temporal, lower nasal, and last the lower temporal meridian at 45° to the horizontal.

To see whether a learning factor had played a significant part in the results we compared the readings taken on different days and found that the variation of responses was independent of the sequence of visits.

Results

The threshold of every position along each meridian was measured, but our analysis was confined to points at 5°, 10°, 15°, 20°, 25°, and 30° from the fovea. The 4 readings at each of these points were averaged and the standard deviation was obtained, except when more than one reading at a point exceeded 1000 asb (see Discussion).

Fig. 1 shows the results from 2 eyes, 1 normal and 1 glaucomatous, without reference to retinal meridian. All other eyes tested gave similar results. As can be seen in both graphs, there is clearly a linear relationship between the log standard deviation and log intensity, showing that as the sensitivity of the retina decreases the variability of responses increases almost linearly. In the graph relating to the normal eye the sensitivity decreases, as expected, towards the periphery. The results from the glaucomatous eye, while showing a similarity in this respect, also show that the variability of responses is not linked

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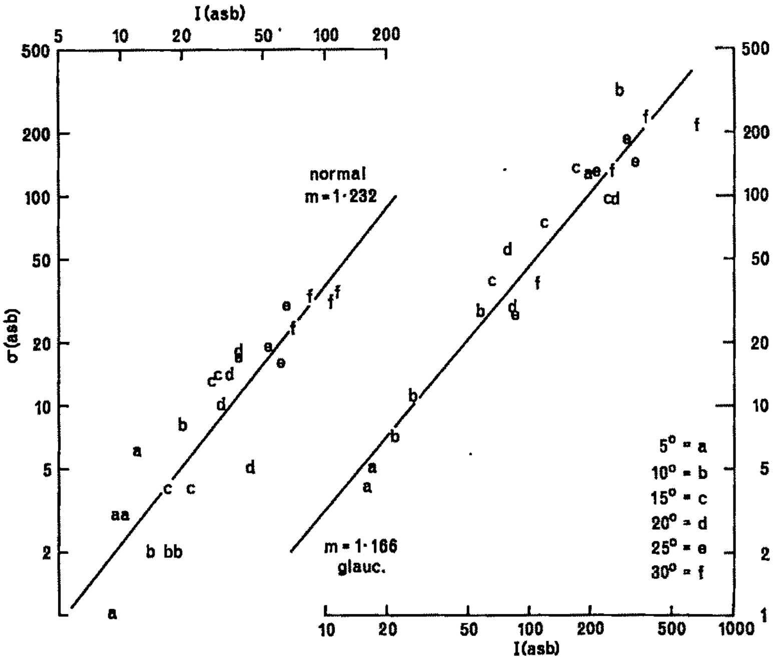


Fig. 1 *Abscissa: threshold target luminance. Ordinate: standard error of the measurement ($N = 4$, but see text). Both quantities are plotted on log scales. The eccentricities are shown in the inset. The* m *values give the slopes of the regression lines. These plots are typical of each of the respective groups of patients*

with retinal position but increases wherever the sensitivity is low owing to damage from the glaucomatous process.

The results from all 3 normal eyes also showed positive correlations between eccentricity, threshold, and variance.

Discussion

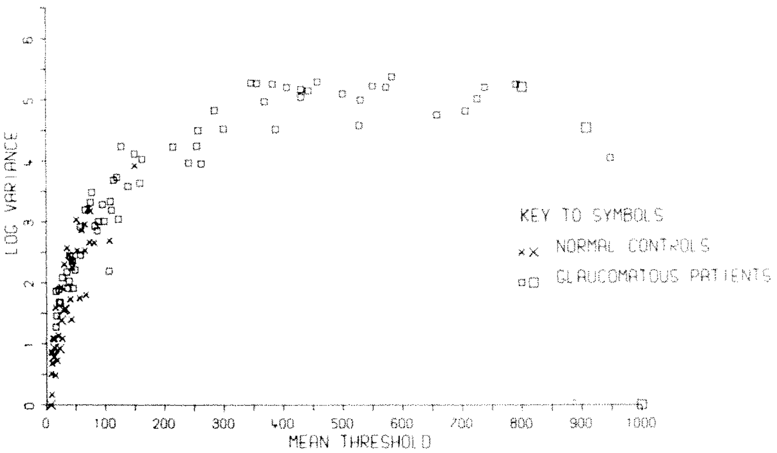
We tried to reduce all artefacts to a minimum and to create the best conditions for visual field testing. Despite this the 3 normal eyes tested showed that as the patient's sensitivity decreases towards the periphery, the variability of responses increases, and it is probable that, had readings been taken beyond 30°, any likely functional change would not have been distinguishable from one due just to chance. The results from the glaucomatous eyes also suggest that it was impossible to predict visual field *changes* using this method for damaged parts of the retina.

Our experiments highlighted the interesting fact that the variability of the patients' responses appeared to be directly related to the sensitivity of the retina, and where the retina was damaged the variability was greatest. This may have a significant bearing on the view that in some cases medication can reduce the size of the defect, and it should make us very wary of all but the grossest change in the defective visual field. The data are sufficiently detailed to enable one to scrutinise them quantitatively.

As any perimetric measurement involves the determination of a visual threshold, clinical tests will be subject at least to the variables affecting such measurements in the laboratory. It is not feasible to subject patients to the rigours of experimental control, and this means that their thresholds will almost certainly be higher than those measured under optimum conditions. In addition we used a non-zero background luminance, which also raises the threshold, the amount varying with the pupil area when this is the limiting aperture. However, both our normal thresholds and their standard deviations are similar to the results obtained by Verriest and Israel (1965) on another instrument, namely, the Goldmann perimeter, and this lends confidence to the belief that our normal observers deserve this epithet.

A variety of theories has been propounded to explain the influence of various parameters on the visual threshold. The best known is due to Hecht *et al.* (1942), who based their interpretation on the quantum nature of light. They argued that weak flashes contain an indeterminable (small) number of light quanta and that the eye will signal 'seen' when a given flash contains a minimum (mean threshold, a) number of quanta or more. In such a situation it is possible to relate the probability, P, seeing a flash of mean intensity, m (absorbed by the

Fig. 2 *The logarithm of the variance (var) as a function of the mean threshold* I *(in asb). Note the constant value of the variance above* I ∼ *250 asb. The zero value for log variances at the extreme ends of the range represent* var = *0. The low value at the upper limit is spurious, and explained in terms of the instrument being unable to deliver more than 1000 asb. (Age spans: Normal, 55 to 62 years; patients, 56 to 62 years)*



retina), when the actual number of quanta is i. It can be shown that

$$P = 1 - \sum_{i=0}^{n-1} e^{-a}(a^i/i!)$$

The relevance of this expression to our results is as follows. The equation is based on the Poisson distribution, a characteristic of which is that the variance and mean are equal. It can be shown that, for the lowest thresholds of our normal observers, this condition is approached. For example, a log mean of 0·92 is associated with a standard deviation, σ, of 0·1 log units. But $\sigma^2 = \text{var}/(n-1)$, where n is the number of observations. Thus var = 4·8 asb, which is of the same order as the mean (antilog of 0·92) = 8·3 asb. A study of the variance is consequently sometimes helpful in selecting one of several possibilities as regards underlying mechanisms.

It should be noted that the data do not obey the predicted relation accurately, and attention is drawn to the fact that the way in which even the normal 'patient' responds to the situation makes this unlikely. In the rigorous tests the probability of seeing a given stimulus is derived from a large number (about 50) presentations. This is impossible in a clinic. In our study the light intensity was increased till the patient said he could see it. We show in the Appendix that this well-known technique makes it theoretically difficult to use it quantitatively to set confidence limits of such narrowness as to enable one to monitor the progress of, or recovery from, retinal disease by its means.

However, the data obtained on the glaucomatous patients lead to a startling conclusion, which is easy to explain on a theoretical basis.

Fig. 1 indicates the large standard deviations recorded by the patients for the defective parts of their visual fields. In some retinal regions the results are so varied as to appear to be purely random and to come from a uniform distribution. It can be shown that, if the readings are made on a continuous scale, the variance of such a distribution is $C^2/12$ where C is the range of possible readings, that is, the gamut of the instrument. If we assume C is 1000 (classing readings greater than the intensity which the instrument can deliver as 1000, which will tend to lower the variance), then the variance for each estimate is $1000^2 \div 12 = 83\,333$, the log of which is 4·92. As shown in Fig. 2, there is close agreement between this predicted and the observed values.

This plot shows that the prediction is fulfilled for 250 apostilbs and above, which is not more than a factor of 10 above likely normal thresholds. We interpret Fig. 2 as meaning that, if a blind person were seated at the perimeter, a similar result would be obtained. This approach provides a clue to its cause: it is likely that the patients were guessing. It is also possible that, because of the smallness of the target, minute eye movements led to a patchy retina, giving rise to a large variation.

Whatever the ultimate explanation of the uniform distribution of readings which we have observed, if our observations are typical they rule out the possibility of obtaining useful confidence limits for those retinal regions for which the mean threshold exceeds about 250 asb. Thus, while perimetry has a diagnostic value in these circumstances, its usefulness as a monitoring device can be overrated.

Appendix

Assume that the intensity of a light flash is increased till the patient signals 'seen'.

The amount of energy at the j^{th} flash, $j = 0, 1, 2 \ldots$

k is fixed as $10^{j/10}$ apostilbs, where $10^{k/10}$ is the last measurable amount of energy ($k = 30$ in this case).

If $X_j = 1$ when the j^{th} flash is seen and 0 otherwise then

$$P(T = m_t) = (\prod_{j=0}^{t-1} p(X_j = 0) \,.\, P(X_t = 1)$$

where T is the recorded threshold and m_t is the energy flashed in experiment, t.

If the number of quanta incident on the cornea at flash j is denoted by m_j, then $p(X_j = 0) = P$ (fewer than n quanta absorbed out of a possible m_j) where n is the number of quanta required for vision.

Assuming Bernoulli trials, that is, that there are two outcomes: either the quantum is absorbed by the retina, with probability, P, or it is not, with probability $1 - P$.

$$P(X_j = 0) = \sum_{r=0}^{n-1} {}^{m_j}C_r \,.\, p^r(1-p)^{m_j - r}$$

Therefore

$$P(T = m_t) =$$

$$\prod_{j=0}^{t-1} [\sum_{r=0}^{n-1} {}^{m_j}C_r\, p^r(1-p)^{m_j - r}] \times$$

$$[\sum_{r=n}^{m_t} {}^{m_t}C_r \,.\, p^r \,.\, (1-p)^{m_t - r}]$$

The mean and variance of this complex probability distribution are not known but it is included in the paper to emphasise the difficulty of using this particular method of perimetry to set confidence limits for future readings on the same area of retina of the same patient. Because of this it is difficult to determine whether the patient's threshold has increased or whether the higher threshold is a purely random variation.

Approximate confidence limits can be calculated for normal retinal parts of patients by first finding the mean and variance for the logged data (this transformation is done to remove the skewness from the data introduced by the fact that the amount of energy was increased exponentially and not linearly), and calculating the confidence intervals as approximately

$$\bar{X} \pm 1{\cdot}96s$$

where $\bar{X}$ is the mean of the logged data and s is the square root of the variance of the logged data. To obtain confidence intervals for the original data, take the antilog of the two values; 95% of future readings should lie within these limits. For example, the readings 40, 50, 50, 100 give a range of between approximately 28 and 123, and the readings 7·9, 7·9, 10, 10 give a range of between 6·8 and 11·6.

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References

Armaly, M. F. (1969). The visual field defect and ocular pressure level in open angle glaucoma. *Investigative Ophthalmology*, **8**, 105–124.

Drance, S. M., Wheeler, C., and Pattullo, M. (1967). The use of static perimetry in the early detection of glaucoma. *Canadian Journal of Ophthalmology*, **2**, 249–258.

Greve, E. L. (1973). *Single and Multiple Stimulus Static Perimetry in Glaucoma; the Two Phases of Visual Field Examination*, pp. 30 and 86. Junk: The Hague.

Goldmann, H. (1945). Grundlagen exakter Perimetrie. *Ophthalmologica*, **109**, 57–70.

Harms, H. (1950). Entwicklungsmöglichkeiten der Perimetrie. *Albrecht von Graefes Archiv für Ophthalmologie*, **150**, 28–57.

Harms, H., and Aulhorn, E. (1959). Vergleichende Untersuchungen über den Wert der quantitativen Perimetrie, Skiaskotometrie und Verschmelzungsfrequenz für die Erkennung beginnender Gesichtsfeldstörungen beim Glaukom. *Documenta Ophthalmologica*, **13**, 303–332.

Hecht, S., Shlaer, S., and Pirenne, M. H. (1942). Energy, quanta and vision. *Journal of General Physiology*, **25**, 819–840.

Sloan, L. (1939). Instruments and techniques for the clinical testing of light senses III. An apparatus for studying regional differences in light sense. *Archives of Ophthalmology*, **22**, 233–251.

Verriest, G., and Israel, A. (1965). Application du périmètre statique de Goldmann au relève topografique de seuils différentiels de luminance pour de petits objects colorés projetés sur un fond blanc. *Vision Research*, **5**, 151–174.

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Isolation of *Chlamydia psittaci* from a patient with interstitial keratitis and uveitis associated with otological and cardiovascular lesions

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SUMMARY A case history of a 15-year-old schoolgirl with fluctuating bilateral uveitis, bilateral stromal keratitis with vascularisation, and bilateral deafness associated with tinnitus and balance disturbance is described. Three years from the onset of her clinical signs she died of a sudden cardiac arrest caused by endocarditis associated with valvular and arterial lesions. *Chlamydia psittaci* was isolated from her conjunctiva. In her blood type-specific antichlamydial antibody at a level of 1/64 against her own isolate was detected. The clinical findings in this patient were suggestive of a Cogan's syndrome. It is highly probable that the chlamydia isolated from the eyes was responsible for her various lesions.

The genus *Chlamydia* comprises the 2 species, *Chlamydia trachomatis* and *C. psittaci*. *C. trachomatis* is responsible for a variety of ocular and genital infections in man (Jones, 1961; Jones, 1964; *Lancet*, 1973; *Lancet*, 1977). *C. psittaci*, which is generally associated with animals, may occasionally cause ocular infections in man (Ostler *et al.*, 1969; Schachter *et al.*, 1968).

In recent years several cases of endocarditis associated with *C. psittaci* have been reported (Levison *et al.*, 1971; Ward *et al.*, 1975). The results of these reports indicate that *C. psittaci* potentially though infrequently is a pathogen for the cardiovascular system and may cause myocarditis as well as valvular lesions (Eisentein and Taubenhass, 1958; Gelfand *et al.*, 1972).

In this report we describe the case of a patient with a longstanding interstitial keratitis and uveitis associated with marked otological symptoms and fatal cardiovascular lesions, from whom a *C. psittaci* agent was isolated.

Case report

A schoolgirl born on 11 August 1957 of Greek-Cypriot extraction was first seen at Moorfields Eye Hospital on 23 August 1972, complaining of intermittent attacks of red, painful, watering eyes during the previous 2 months. Each eye had a visual acuity of 6/6. In the right eye there was hyperaemic bulbar conjunctiva and anterior uveitis with a mild degree of flare and cells in the anterior chamber, but no abnormality in the fundus. The left eye appeared normal. She was treated with topical dexamethasone eye drops with temporary benefit.

The uveitis pursued a fluctuating course involving either eye at first and soon both eyes, though she was under treatment with a variety of topical steroid eye drops including dexamethasone, prednisolone, and Betnesol. Towards the end of 1973 she developed a persistent bilateral keratitis.

The keratitis was at first mild and peripheral, but soon became central and fluctuated between a diffuse central stromal haze and coarse granular midstromal lesions (Figs. 1 and 2) and a disciform keratitis with vascularisation (Fig. 3). Later she developed some granular lipid deposition (Fig. 3).

In November 1974 she was admitted to the Royal Northern Hospital, London, for further investigations. After extensive laboratory tests (see laboratory investigations) both sarcoidosis and collagen vascular disease were excluded, and she was then discharged from the hospital on treatment with indomethacin 25 mg 3 times a day.

On 28 December 1974 the patient was referred to the Royal Northern Ear, Nose and Throat Hospital

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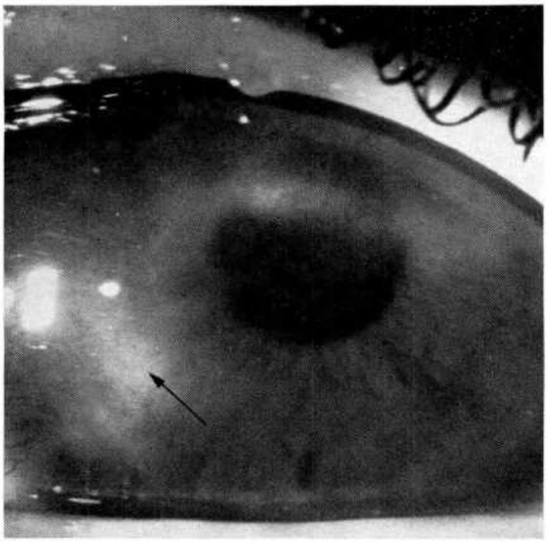

Fig. 1 *Diffuse stromal keratitis*

because of sudden onset of bilateral deafness, tinnitus, and balance disturbance. The deafness was of moderate severity and appeared to be symmetrical. The tinnitus took the form of a bilateral constant high pitched buzzing, and the balance disturbance, which had initially been an acute rotational vertigo, had become a constant feeling of unsteadiness, especially on sudden head movement, and it was not associated with nausea or loss of consciousness.

Clinical examination showed normal tympanic membranes, bilateral Rinne test positive, Weber test central, normal cranial nerve examination and no spontaneous nystagmus or papilloedema. There was obvious unsteadiness of gait. Pure tone audiometry showed bilateral sensorineural deafness (see Fig. 4). There was bilateral poor speech discrimination. The Bekesy audiogram was type 1. No tone decay could be demonstrated. The short increment sensitivity test (SISI) showed 60% response at 1000 Hz and 80% at 2000 Hz. Mastoid *x*-rays and *x*-rays of the internal auditory meatuses were normal. The positional test was negative. Caloric stimulation showed a symmetrical and equal response with no evidence of canal paresis or marked directional preponderance. Electronystagmography showed no evidence of spontaneous nystagmus or any other abnormality. Electrocochleography confirmed the hearing thresholds found on pure tone audiometry. The eighth nerve action potential was of normal form.

The patient was admitted to hospital on 8 January 1975 and started on systemic prednisolone 25 mg 3 times a day, tailing off to a maintenance dose of

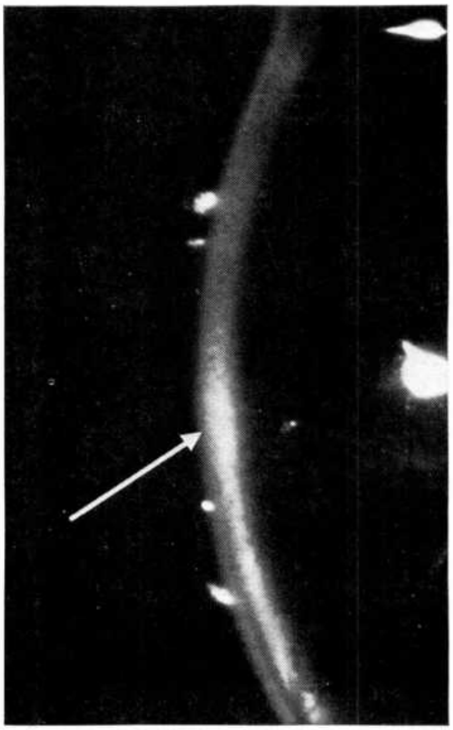

Fig. 2 *Diffuse stromal keratitis in the narrow slit-lamp beam* (×10)

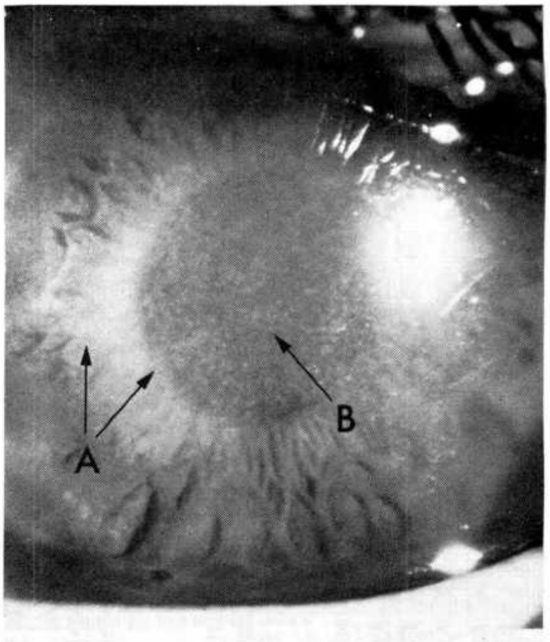

Fig. 3 *Diffuse stromal keratitis* (A) *and granular lipid deposition* (B) (×7)

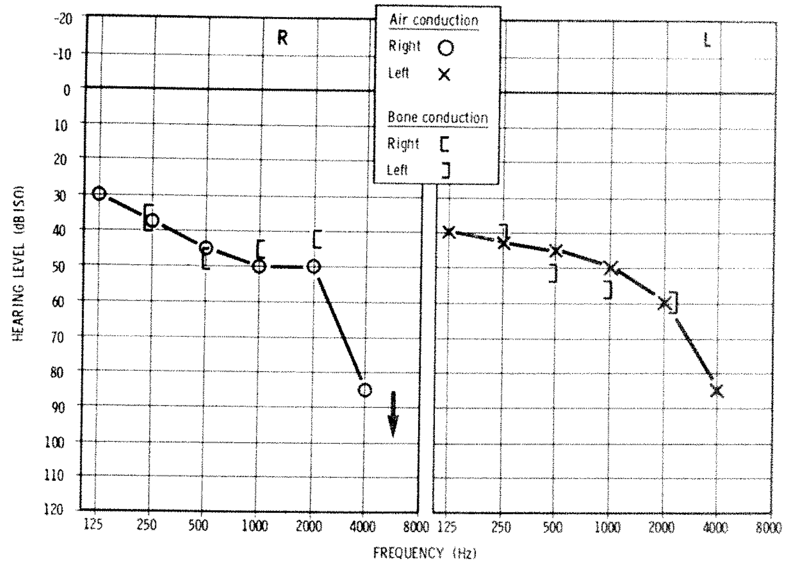

Fig. 4 *Pure-tone audiogram obtained on 30 December 1974, showing a moderate symmetrical sensorineural hearing loss throughout the frequency range tested*

2·5 mg 3 times a day over 2 weeks. This failed to ameliorate the otological symptoms. Over the next 10 months the deafness and tinnitus pursued a fluctuating course, but always relapsing to near their severity on presentation. The constant feeling of unsteadiness persisted with occasional exacerbations during the period of observation. However, several months later it was revealed by her father that she might have exceeded the recommended dose of indomethacin on a single occasion, though it was not clear by how much.

In February 1975 a *C. psittaci* agent was isolated from a conjunctival swabbing taken during one of the exacerbations of keratouveitis because of the resemblance to Reiter's disease. After this the patient was treated with a course of doxycycline 300 mg as an initial dose followed by 100 mg daily for 3 weeks. There was then a definite decrease in the intensity of the ocular signs and the number of recurrences of keratouveitis. A similar course of treatment was repeated 2 months later.

After the isolation of chlamydia from the eye it was disclosed that the family cat had been suffering from an ocular infection, associated with discharge, about the time of the onset of the patient's symptoms. However, clinical and laboratory tests on this cat for chlamydial or viral infections were all negative.

A clinical examination of the genital tract carried out by Dr E. M. C. Dunlop, Diagnostic Clinic, Moorfields Eye Hospital, showed no abnormality.

On 4 November 1975 the patient was admitted as an emergency to Plaistow Hospital with severe chest pain at rest. For the previous 7 days there had been an increasing dyspnoea on effort. An electrocardiogram showed widespread changes in lead II and lead V2-6. Two hours after admission the patient died of sudden cardiac arrest despite vigorous resuscitation efforts.

NECROPSY

A coroner's necropsy was carried out by Dr Alan Grant, of Guy's Hospital, on 5 November 1975. It was found that in the aortic valve area were many layers of fibrin with organisation producing thickening, but weakening of the aortic cusps with herniation of 2 of these. There were also loose deposits of fibrin proximal to the valve ring. Histologically the proximal segments of the coronary arteries showed destruction of the arterial walls. There was thickening of the intima and media of the sinus of Valsalva, with many neutrophils in the media, but mainly lymphocytic infiltration of the intima. There was an atrial destructive arterial lesion which could have been embolic or inflammatory. The aorta showed destruction of the intima and the media. The ostia of the coronary arteries were all narrowed by fibrin deposits. Histological and gross examination of other organs showed no abnormality. Unfortunately, because death occurred unexpectedly and in a hospital where no past records were available, sections of the eyes and internal ears were not taken at the necropsy, and no material was obtained for detection of chlamydia from the various cardiac and other lesions.

LABORATORY INVESTIGATIONS

Repeated haematological and biochemical tests showed no abnormality. The levels of blood sugar, urea, cholesterol, calcium, triglycerides, and electrolytes were normal. Liver function tests showed no abnormality. The erythrocyte sedimentation rate was persistently raised to between 30 mm and 42 mm in the first hour. *X*-rays of the chest and sinuses were normal, but *x*-ray of the spine showed definite changes in the sacroiliac joints suggestive of ankylosing spondylitis. The Kveim test was negative, as was the Mantoux to 1/1000 in spite of recent BCG vaccination. The rheumatoid arthritis latex test and autoantibody screening were negative. Tests for syphilis including Cardiolipin Wassermann, Venereal disease reference laboratory flocculation test, Reiter's protein complement fixation test, Treponema pallidum haemagglutination test, Treponema pallidum immobilisation test, and Absorbed fluorescent treponemal antibody test were all negative in both the patient and her parents. Examination of cerebrospinal fluid was normal and the CSF Wassermann reaction was negative.

Serum IgM was found to be raised on 3 separate occasions: 245 mm/ml on 3 December 1973, 255 mm/ml on 15 April 1974, and 330 mm/ml on 19 May 1975. Other serum immunoglobulin concentrations were normal.

Repeated tests from the eyes for virus isolation were all negative. Complement fixation tests showed no increase in the titre of antibody against herpes simplex, varicellazoster, adenovirus, and mumps virus.

The micro-IF test (Wang and Grayston, 1971; Treharne *et al.*, 1972) on the serum obtained on 9 May 1974 showed type-specific antichlamydial antibody at a level of 1/64 against an atypical chlamydia (IOL-207) (Dwyer *et al.*, 1972; Treharne *et al.*, 1972). The level of antichlamydial antibody in this serum against various serotypes of *C. trachomatis* or *C. psittaci* included in the test (Dwyer *et al.*, 1972; Treharne *et al.*, 1972) was 1/8 or lower. A repeat micro-IF test on 4 February 1975 showed the type-specific antichlamydial antibody at a level of 1/32. Micro-IF tests of the sera obtained from this patient in April, May, and September of 1975 consistently showed a level of 1/64.

In February 1975, after inoculation of a conjunctival specimen collected during an acute exacerbation of keratouveitis into the yolk sac of fertile eggs (Gordon *et al.*, 1969) a chlamydial strain (CPs/GB/IOL-1959/0) was isolated. Inoculation of the egg-grown isolate into irradiated McCoy cells produced intracytoplasmic inclusion bodies similar to those of *C. psittaci*. The isolate produced iodine-negative inclusions in cell culture (Gordon and Quan, 1965) and was resistant to sulphadiazine (Lin and Moulder, 1966). Serotyping by a micro-IF test (Wang *et al.*, 1971) showed that this isolate was not identical with IOL-207, guinea-pig inclusion conjunctivitis agent, feline keratoconjunctivitis agent, iodine-negative lymphogranuloma venereum agent—33-L (Treharne *et al.*, 1972), bovine enzootic abortion of ewes (A22/18), and a strain of *C. psittaci* isolated from the eye of a patient with follicular conjunctivitis (IOL-395/0). Further characterisation of this isolate is continuing.

Repeated inoculation of irradiated McCoy cell culture (Darougar *et al.*, 1970) and the yolk sac of fertile eggs with specimens collected from the conjunctiva, cornea, urethra, the genital tract, and rectum were all negative.

Micro-IF testing of various samples of sera from this patient using antigens prepared from IOL-207 and her own isolate (IOL-1959) showed a similar titre of antibody (1/64) against both antigens.

With an indirect immunofluorescent staining technique no chalmydial antigens were detected in tissues obtained from the heart, liver, and kidneys that were fixed with formalin for over a year.

Discussion

The case described above presents several unusual features. The clinical picture of interstitial keratitis and uveitis raised the possibility of several diseases, namely, herpetic or syphilitic infections, Reiter's disease, Vogt-Koyanagi-Harada or Cogan's syndromes, or sarcoidosis. Treatment with topical steroids appeared to have temporary beneficial effect. A good response of the keratouveitis was observed with doxycycline therapy.

Otological symptoms of fluctuating sensorineural hearing loss, tinnitus, and vertigo are suggestive of Menière's syndrome, as distinct from Menière's disease. This is a symptom complex which may be due to a number of disease entities, including Menière's disease itself, the Vogt-Koyanagi-Harada syndrome, Cogan's syndrome, late congenital syphilis, and trauma (perilymph leak (Hinchcliffe, 1973)).

This patient had been treated with indomethacin. The patient's father claimed a few months later that otological symptoms followed her taking an excess dose of indomethacin on one occasion. Sensorineural deafness has occasionally been suggested as a rare side effect of indomethacin treatment (Robinson, 1965; Kinsella *et al.*, 1967). However, other studies have shown that the central nervous system side effects of indomethacin were of a transient nature without sequelae, disappearing completely on cessation of the drug (Rothermich, 1966, 1973). In this patient, although indomethacin was discontinued soon after the onset of the otological symptoms, her clinical condition did not improve over the subsequent months.

The extensive laboratory tests and *x*-rays had ruled out syphilis, sarcoidosis, or collagen vascular disease as the cause of ocular and otological lesions. In the absence of alopecia, vitiligo, and fundus abnormality the diagnosis of Vogt-Koyanagi-Harada syndrome could not be sustained.

The chronic fluctuating stromal keratitis and vascularisation of the cornea associated with deafness and cardiovascular abnormalities are highly suggestive of Cogan's syndrome (Eisentein and Taubenhass, 1958; Duke-Elder, 1965; Seel, 1972), though it is difficult to exclude the diagnosis of Reiter's disease because of the associated sacroiliac arthritis. The persistently raised levels of the ESR and IgM in the blood indicated that an infection might be responsible for her various signs. Detection of type-specific antichlamydial antibody by a micro-IF test in her sera and the isolation of a *C. psittaci* agent from her eyes strongly suggested that chlamydia might be the causative organism.

C. psittaci infection has been shown to be associated with endocarditis. Levison *et al.* (1971) described 2 cases of endocarditis due to *C. psittaci* causing prominent finger-like vegetations of the heart valve. Ward *et al.* (1975) discussed 3 patients with *C. psittaci* endocarditis, 2 of whom died and 1 of whom needed aortic valve replacement. Prominent friable granulations on the heart valve were again a feature of these cases. Regan *et al.* (personal communication) describe a case of *C. psittaci* endocarditis associated with glomerulonephritis in a patient with a history of prolonged contact with cats and a high level of type-specific IgG and IgM against feline keratoconjunctivitis agent (*C. psittaci*).

In our patient, in the absence of examination of the temporal bones and failure to demonstrate chlamydial antigens in cardiovascular tissues, it is difficult to be as certain about the aetiology of the otological and cardiovascular lesions as about that of the ocular lesions. However, it seems highly probable that these lesions were also caused by the same underlying disease process.

The result of this study suggests that a possible *C. psittaci* infection should always be considered in the diagnosis of any obscure keratouveitis, endocarditis, or Menière's syndrome.

This complicated case was dealt with by many physicians and surgeons in various London hospitals. We thank in particular Dr E. M. C. Dunlop, Mr B. Jay, of the Moorfields Eye Hospital, Mr J. B. Booth of the London Hospital, Dr G. James of the Royal Northern Hospital, and Dr A. Grant of Guy's Hospital for their assistance in preparing this report.

References

Darougar, S., Kinninson, J. R., and Jones, B. R. (1970). Simplified irradiated McCoy cell-culture for isolation of Chlamydiae. In *Trachoma and Related Disorders Caused by Chlamydial Agents*, pp. 63–70. Excerpta Medica International Congress Series No. 223.

Dwyer, R. St. C., Treharne, J. D., Jones, B. R., and Herring, J. (1972). Results of micro-immunofluorescence test for the detection of type-specific antibody in certain chlamydial infections. *British Journal of Venereal Diseases*, **48**, 452–459.

Duke-Elder, S. (1965). *System of Ophthalmology*, Vol. 8, p. 838. Henry Kimpton: London.

Eisentein, B., and Taubenhass, M. (1958). Non-syphilitic interstitial keratitis and bilateral deafness (Cogan's syndrome) associated with cardiovascular disease. *New England Journal of Medicine*, **258**, 1074–1079.

Gelfand, M. L., Kantor, T., and Gorstein, F. (1972). Cogan's syndrome with cardiovascular involvement: aortic insufficiency. *Bulletin of the New York Academy of Medicine*, **48**, 647–660.

Gordon, F. B., Harper, I. A., Quan, A. L., Treharne, J. D., Dwyer, R. St.C., and Garland, J. A. (1969). Detection of Chlamydia (Bedsonia) in certain infections in man. I. Laboratory procedures: Comparison of yolk sac and cell culture for detection and isolation. *Journal of Infectious Diseases*, **120**, 451–462.

Gordon, F. B., and Quan, A. L. (1965). Occurrence of glycogen in inclusions of the psittacosis-lymphogranuloma venereum-trachoma agents. *Journal of Infectious Diseases*, **115**, 186–196.

Hinchcliffe, R. (1973). In *Recent Advances in Otolaryngology*, p. 127. Churchill, Livingstone: Edinburgh and London.

Jones, B. R. (1961). Trachoma and allied diseases of the eye. *Transactions of the Ophthalmological Society of United Kingdom*, **81**, 367–378.

Jones, B. R. (1964). Ocular syndromes of TRIC-virus infection and their possible genital significance. *British Journal of Venereal Diseases*, **40**, 3–18.

Kinsella, T. D., Mackenzie, K. R., Kim, S. O., and Johnson, L. G. (1967). Evaluation of indomethacin by a controlled, cross-over technique in 30 patients with ankylosing spondylitis. *Canadian Medical Association Journal*, **96**, 1454–1459.

Lancet, Editorial (1973). Chlamydiae and genital infection. *Lancet*, **1**, 703.

Lancet, Editorial (1977). Chlamydial infections of the eye. *Lancet*, **2**, 857–858.

Levison, D. A., Ward, C., Gurthrie, W., Green, D. M., and Robertson, P. G. C. (1971). Infective endocarditis as part of psittacosis. *Lancet*, **2**, 844–847.

Lin, H. S., and Moulder, J. W. (1966). Patterns of response to sulfadiazine, D-cycloserine and D-alanine in members of the psittacosis group. *Journal of Infectious Diseases*, **116**, 372–376.

Ostler, H. B., Schachter, J., and Dawson, C. R. (1969). Acute follicular conjunctivitis of epizootic origin. *Archives of Ophthalmology*, **82**, 587–591.

Regan, R. J., Dathan, J. R. E., and Treharne, J. D. (1977). Personal communication.

Robinson, R. G. (1965). Indomethacin in rheumatic disease—a clinical assessment. *Medical Journal of Australia*, **1**, 266–269.

Rothermich, N. O. (1966). An extended study of indomethacin: I. Clinical pharmacology. *Journal of the American Medical Association*, **195**, 531–536.

Rothermich, N. O. (1973). Correspondence. *Journal of the American Medical Association*, **226**, 1471–1472.

Schachter, J., Arnstein, P., Dawson, C. R., and Hanna, L. (1968). Human follicular conjunctivitis caused by infection with a psittacosis agent. *Proceedings of the Society of Experimental Biology and Medicine*, **127**, 292–295.

Seel, J. (1972). Cogan's syndrome. Interstitial keratitis with sudden deafness. *Albrecht v. Graefes Archiv klinische und experimentelle Ophthalmologie*, **185**, 281–287.

Treharne, J. D., Davey, S. J., Gray, S. J., and Jones, B. R. (1972). Immunological clasification of TRIC agents and of some recently isolated LGV agents by the micro-immunofluorescence test. *British Journal of Venereal Diseases*, **48**, 18–25.

Wang, S. P., and Grayston, J. T. (1971). Immunological relationships between genital TRIC, LGV and related organisms in a new micro titre—indirect immunofluorescence test. *American Journal of Ophthalmology*, **70**, 367–374.

Ward, C., Sagar, H. J., Cooper, D., and Ward, A. M. (1975). Insidious endocarditis caused by *Chlamydia psittaci*. *British Medical Journal*, **4**, 734–735.

British Journal of Ophthalmology, 1978, **62**, 715–721

Fuchs's heterochromic cyclitis: a simultaneous bilateral fluorescein angiographic study of the iris

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SUMMARY Twelve patients with Fuchs's heterochromic cyclitis (FHC) were studied with simultaneous bilateral fluorescein angiography of the iris. The flow began a little earlier in the contralateral iris in 4 cases, and simultaneously in both irides in 8 cases. The radial iris vessels were narrow in 7 eyes with FHC and in the contralateral eyes of 2 elderly patients and of 1 patient with pigmentary retinal dystrophy and FHC. An ischaemic sector of the iris was seen in 6 eyes with FHC, neovascularisation of the iris in 8 eyes, and fluorescein leakage of the iris vessels was seen in all eyes with FHC. No neovascularisation of the iris occurred in the contralateral eyes, and only minimal fluorescein leakage was seen at the pupillary border of 5 contralateral eyes. The results support the hypothesis of vascular pathomechanism in FHC.

The clinical picture of Fuchs's heterochromic cyclitis (FHC) is well known (Fuchs, 1906; Duke-Elder and Perkins, 1966; Loewenfeld and Thompson, 1973). However, the aetiology of FHC is still in doubt (Duke-Elder and Perkins, 1966). An eye with FHC shows increased penetration of fluorescein from the blood stream into the anterior chamber (Amsler and Huber, 1946), and a small filiform haemorrhage may occur after paracentesis (Amsler and Verrey, 1946). A delicate rubeosis was noted histologically on the anterior surface of the iris and over the entire circumference of the angle in an eye with FHC (Perry *et al.*, 1975). Fluorescein angiograms have demonstrated abnormal iris vessels with diffuse or patchy leakage of the dye from these vessels (Loewenfeld and Thompson, 1973). The purpose of this study was to evaluate further the vascular component in FHC. We report our observations on the circulation and vascular pattern of both irides in FHC studied by simultaneous bilateral fluorescein angiography of the anterior eye.

Patients and methods

Twelve patients with FHC were included in this study. Clinical characteristics of the first 11 patients (Cases 1–11) have been described earlier (Saari *et al.*, 1977) and the case numbers of these patients correspond to those in the earlier study. The 12th patient in this study was a 39-year-old man with keratic precipitates, aqueous cells, complicated cataract, and stromal and pigment epithelial atrophy of the iris in the left eye, which was lighter in colour than the right eye with normal iris structure. He had pigmentary retinal dystrophy in both eyes.

Simultaneous bilateral angiography of the anterior eye (Helve and Nieminen, 1974) was performed on all patients. The photographic apparatus consisted of a Zeiss biomicroscope in which 2 motor-driven Nikon cameras were connected with one another. By means of prisms both eyes were photographed simultaneously. We used a pair of a Baird Atomic inteference filters B4 and as the barrier Kodak Wratten filters No 15. For each angiography we used 0·043 ml/kg of 10% sodium fluorescein. Photographs were taken at 0·8-second intervals. In each angiogram the beginning of the flow, the vascular pattern, the presence of ischaemic areas and neovascularisation, and the source of fluorescein leakage were recorded and compared with the findings of the contralateral eye.

Results

Simultaneous bilateral fluorescein angiographic findings from the iris in the eyes with FHC and in the contralateral eyes are shown in Table 1. In 3 patients (Cases 1–3) the flow in the anterior part

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Table 1 *Simultaneous bilateral iris fluorescein angiographic findings in eyes with Fuchs's heterochromic cyclitis (FHC) and in contralateral eyes*

Case No.	*Age*	*Eye*	*Beginning of flow*	*Radial iris vessels*	*Ischaemic sector*	*Neovascularisation*		*Fluorescein leakage*	
						PP	*CP*	*PP*	*CP*
1	43	R (FHC)		Narrow, straightened	12	++	+	++	+
		L	L	Normal	Coloboma	–	–	PB	–
2	38	R	R	Normal	–	–	–	PB	–
		L (FHC)		Narrow, straightened	2–4	++	++	++	++
3	59	R (FHC)		Narrow, straightened	½9–½10	++	++	++	++
		L	L	Normal	–	–	–	PB	–
4	12	R	R	Normal	–	–	–	–	–
		L (FHC)		Normal	–	–	–	+	
5	15	R	R=L	Normal	–	–	–	–	–
		L (FHC)		Narrow, straightened	3–4, 6–7	–	+	+	+
6	57	R (FHC)		Narrow	–	–	–	++	–
		L	R=L	Narrow	–	–	–	–	–
7	71	R	R=L	Narrow	–	–	–	–	
		L (FHC)		Narrow	–	+	+	++	+
8	51	R	R=L	Normal	–	–	–	PB	–
		L (FHC)		Normal	½3–6–10	+	+	++	++
9	35	R	R=L	Normal	–	–	–	–	–
		L (FHC)		Normal	–	–	–	+	–
10	27	R	R=L	Normal	–	–	–	PB	–
		L (FHC)		Normal	–	++	++	++	++
11	42	R (FHC)	R=L	Dilated	–	–	–	+	+
		L		Normal	–	–	–	–	–
12	39	R	R=L	Narrow	–	–	–	–	–
		L (FHC)		Narrow	7–12–3	–	+	+	+

PP = pupillary part of the iris. CP = ciliary part of the iris. PB = pupillary border. ++ = extensive. + = moderate. – = absent

of the eye with FHC was slightly more delayed than in the contralateral eye (Fig. 1 *A*, *B*). The eyes with FHC showed narrow, straightened radial iris vessels, an ischaemic iris sector, and neovascularisation with leakage in the pupillary and ciliary parts of the iris (Figs. 1–2), while the contralateral eyes showed normal vascular pattern of the iris without any ischaemia or neovascularisation (Fig. 1 *B*) and only scanty fluorescein leakage at the pupillary border. In a 12-year-old boy (Case 4) the flow was slightly delayed in the anterior part of the eye with FHC, showing fluorescein leakage near the pupillary margin.

In 8 patients (Cases 5–12) the flow began simultaneously in the anterior part of both eyes (Fig. 3 *A*, *B*). In a 15-year-old boy (Case 5) the eye with FHC showed narrow and straightened radial iris vessels, ischaemic iris sectors, moderate neovascularisation with leakage in the ciliary part of the iris and leakage of fluorescein in the pupillary part of the iris, whereas the angiographic findings in the contralateral iris were normal. In three patients (Cases 8–10) the breadth of the radial iris vessels was bilaterally normal; the iris of the eyes with FHC showed moderate fluorescein leakage near the pupillary margin (Case 9), an ischaemic sector (Case 8), and moderate (Case 8) or extensive (Case 10) neovascularisation with extensive fluorescein leakage in the ciliary and pupillary parts of the iris (Figs. 3, 4). The angiographic findings in the contralateral iris were normal except for minimal fluorescein leakage at the pupillary border (Fig. 3 *F*, *H*) in 2 cases (8, 10). A 42-year-old man (Case 11) showed dilated radial iris vessels and moderate fluorescein leakage in the ciliary and pupillary parts of the iris in the eye with FHC; the angiographic findings in the contralateral iris were normal.

In 2 elderly patients the angiograms revealed narrow radial iris vessels in both eyes; extensive fluorescein leakage was seen in the pupillary part (Cases 6, 7) and moderate fluorescein leakage in the ciliary part (Case 7) of the iris in the eye with FHC (Fig. 5). In the patient with pigmentary retinal dystrophy in both eyes (Case 12) the radial iris vessels were bilaterally narrow; the eye with FHC showed a large ischaemic iris sector, neovascularisation in the ciliary part, and fluorescein leakage in the pupillary and ciliary parts of the iris.

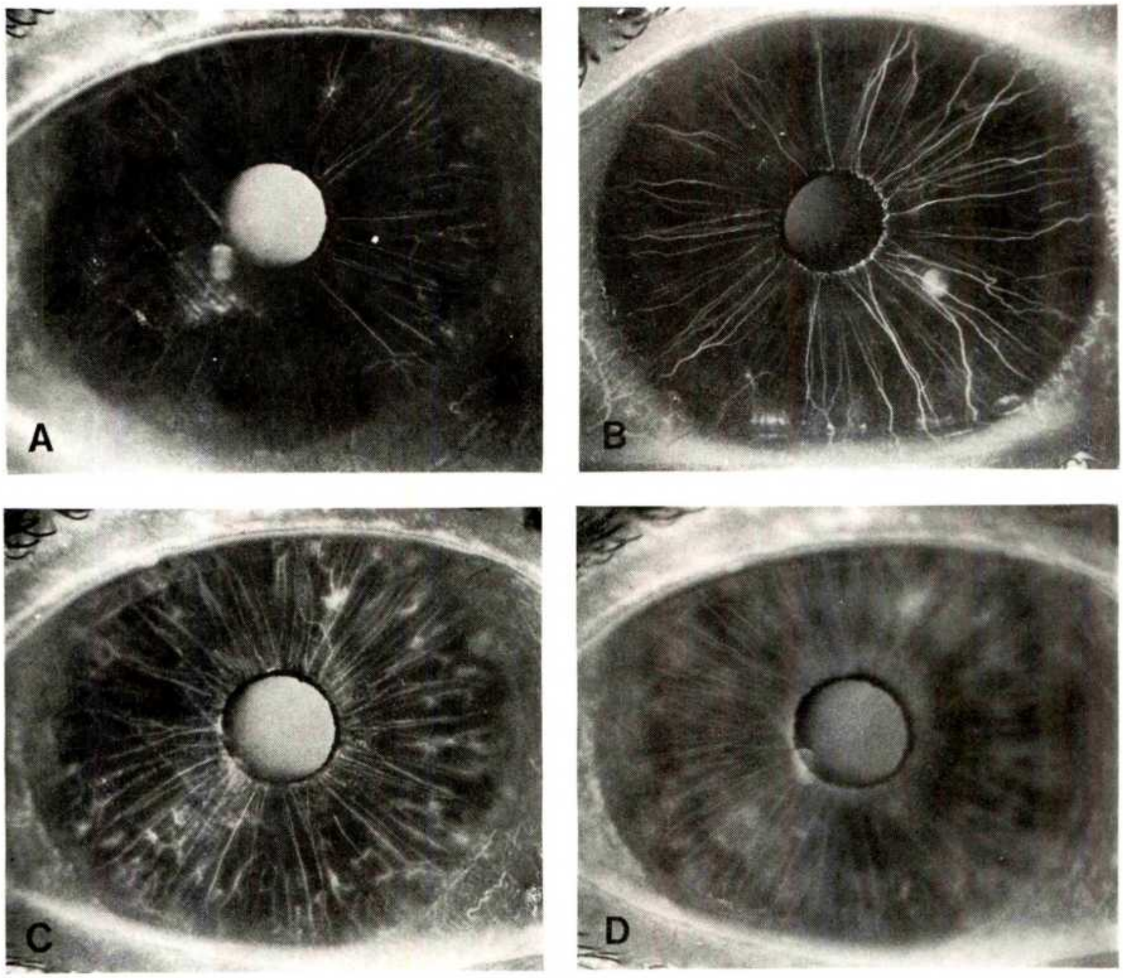

Fig. 1 (A, B) *Simultaneous bilateral iris angiogram in FHC (Case 3) showing* (A) *affected eye with beginning of flow in radial iris arteries and in neovascular tufts of ciliary part, and* (B) *contralateral eye with normal iris vasculature in arteriovenous phase.* (C, D) *Affected eye* (C) *6·4 s later showing narrow radial iris vessels and pronounced neovascularisation, and* (D) *12 s later showing diffuse leakage*

Discussion

Conventional iris angiograms in heterochromia may be difficult to interpret (Amalric, 1971). We used simultaneous bilateral iris angiography, which permits following the flow in both eyes and direct comparison of changes in the affected eye with the normal contralateral eye.

Simultaneous bilateral iris angiograms revealed in this study a slightly delayed iris circulation in 4 eyes and narrow radial iris vessels in 7 eyes with FHC. Histopathological studies have shown in FHC thickening and hyalinisation of the walls of the iris vessels, with proliferation of the endothelium reducing the lumen (Georgiades, 1964). We found ischaemic iris sectors as a sign of defective iris perfusion in 6 eyes with FHC. The slowing of iris circulation, narrow radial iris vessels, and ischaemic iris sectors seen in this study suggest that there is anterior segment ischaemia in eyes with FHC.

Simple biomicroscopic examination does not reveal neovascularisation of the iris in FHC (Campinchi, 1973). In this study angiograms revealed neovascularisation of the iris in 8 eyes with FHC. It was associated with an ischaemic iris sector in 6 cases and was most prominent in the eyes with narrow and straightened radial iris vessels. Thus anterior ocular ischaemia occurred in most eyes

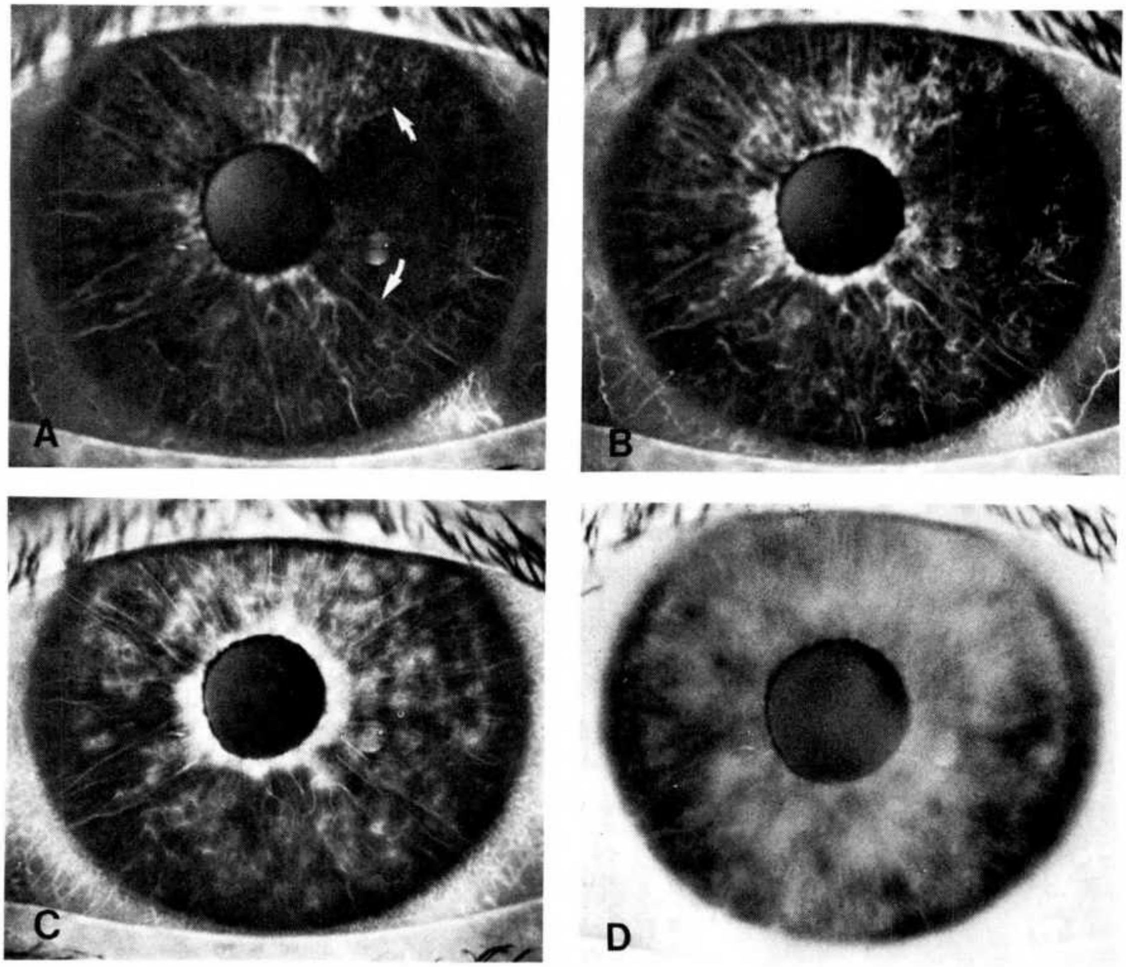

Fig. 2 *Iris angiogram in FHC (Case 2).* (A) *Narrow radial iris arteries, ischaemic iris sector* (arrows), *and* (B) *extensive neovascularisation which* (C) *leak fluorescein.* (D) *Diffuse leakage in late phase*

with FHC and neovascularisation of the iris.

In this study all eyes with FHC showed fluorescein leakage of the iris vessels. Leakage was most prominent at the site of newly-formed vessels, but it was also seen in 4 cases (4, 6, 9, 11) without neovascularisation. These findings are in good agreement with Amsler and Huber's (1946) observations on increased fluorescein permeability of blood-aqueous barrier in FHC. Sclerosis and hyalinisation of the iris vessels and neovascularisation may explain also the vascular fragility seen in FHC as filiform haemorrhage on puncture of the anterior chamber.

The angiographic findings in the iris in different eyes with FHC showed some variations. This may be explained on the basis of different age of the patients and different grade and stage of the disease. The present results suggest that at the beginning of the disease there is leakage at the pupillary border and near the pupillary margin (Case 4). Later the radial iris vessels may become narrow and straightened with an ischaemic iris sector (Case 5), and in a late stage neovascularisation and extensive leakage are seen.

The present results support the hypothesis of a vascular pathomechanism in FHC. Flare and cells in the anterior chamber, iris atrophy with rubeosis, and cataract have been experimentally produced by occluding the long posterior or anterior ciliary arteries (Vassileva *et al.*, 1975). We have seen cases in which signs similar to those in FHC have followed surgery for retinal detachment or squint, or recurrent necrotising rheumatic scleritis. The patho-

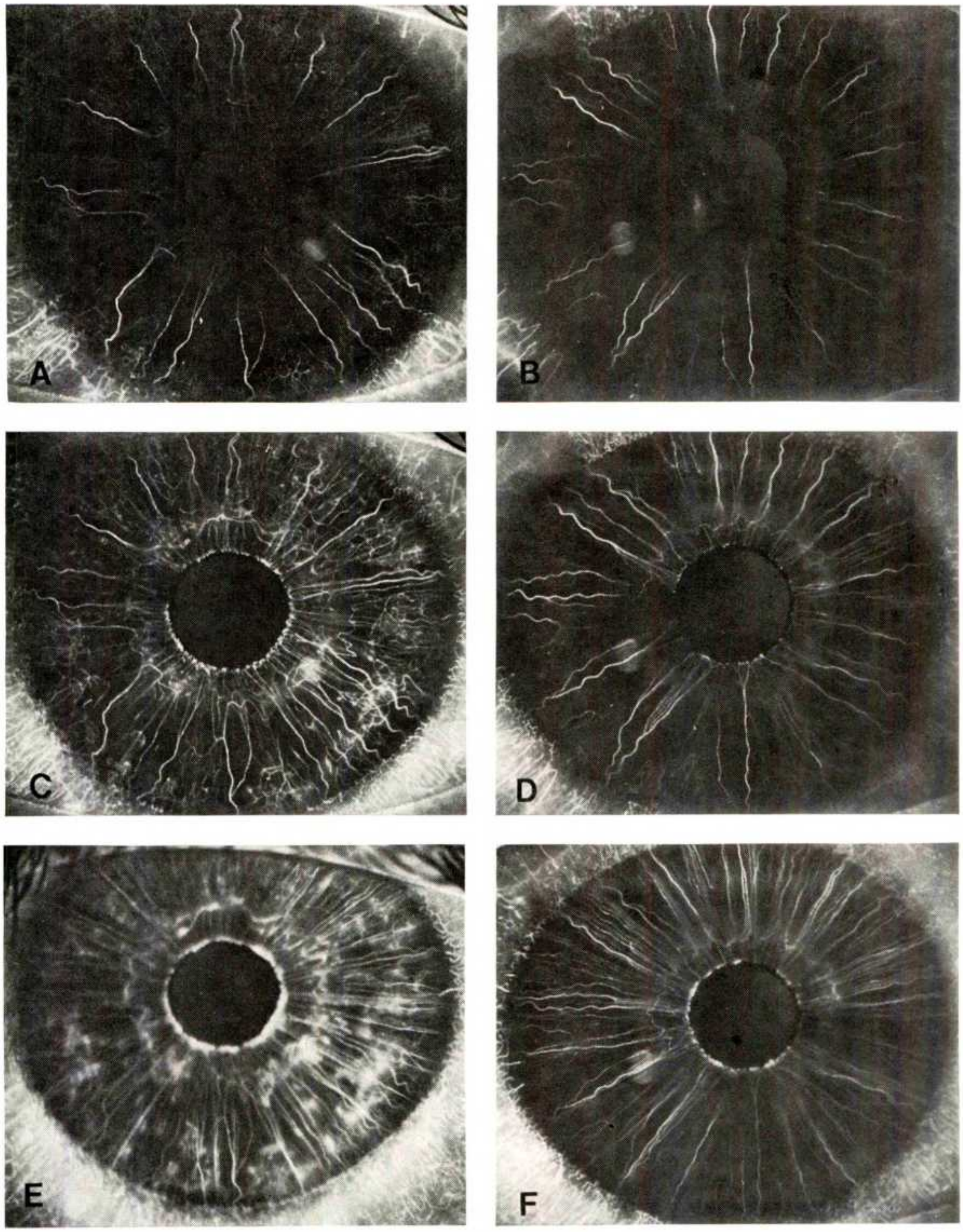

Fig. 3 *Simultaneous bilateral iris angiogram in FHC (Case 10)* (A, B) *Arterial phase showing* (A) *affected iris with radial arteries of normal breadth and neovascularisation in ciliary part, and* (B) *contralateral iris with normal radial arteries.* (C, D) *Arteriovenous phase showing* (C) *affected iris with neovascularisation in pupillary and ciliary parts, and* (D) *contralateral iris with normal vascular pattern.* (E, F) *Late venous phase showing* (E) *affected iris with fluorescein leakage from new vessels, and* (F) *contralateral iris with normal radial veins*

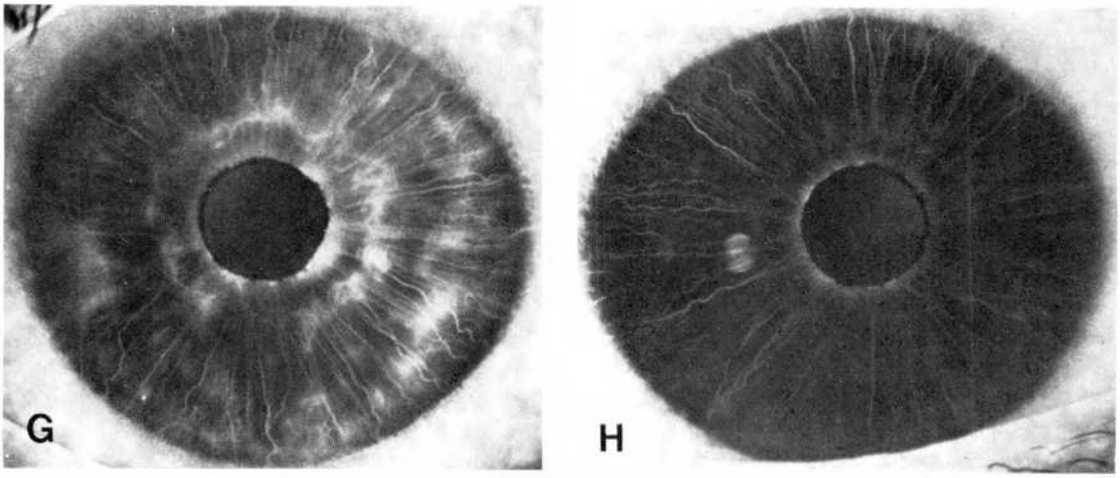

Fig. 3 (G, H) *Late phase showing* (G) *affected iris with diffuse leakage, and* (H) *contralateral iris with scanty leakage at pupillary border*

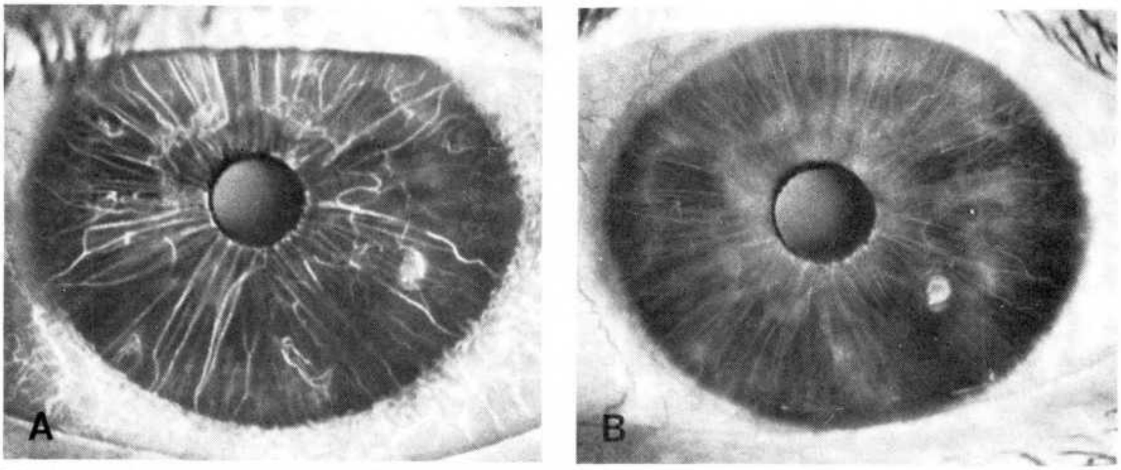

Fig. 4 *Iris fluorescein angiogram in FHC (Case 8) showing* (A) *neovascularisation, and* (B) *18·4 s later, leakage of dye from new vessels*

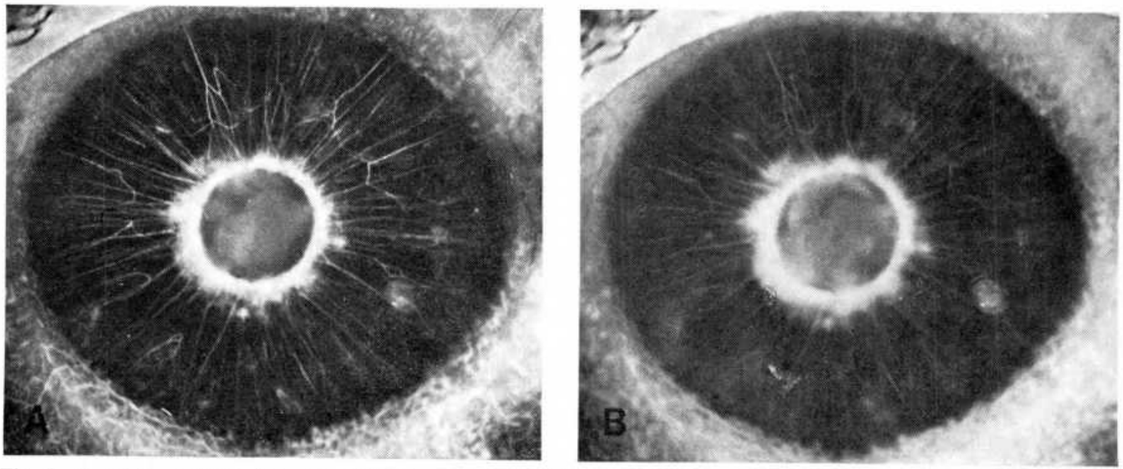

Fig. 5 *Iris fluorescein angiogram in FHC (Case 7).* (A) *Narrow radial iris vessels and neovascularisation.* (B) *8·8 s later, extensive leakage around the pupil and leakage of dye from new vessels in ciliary part*

mechanism in these cases was obviously the interruption of the blood supply to the anterior segment. Because the iris vessels are purely sympathetically innervated (Ehringer and Falck, 1966), dysfunction of the sympathetic innervation of the iris on a hereditary basis may explain the pathogenesis in FHC.

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References

Amalric, P. (1971). Discussion of the paper L'Hétérochromie de l'iris by J. Michiels and J. P. Dernouchamps. *Bulletins et mémoires de la Société Française d'Ophthalmologie*, **84**, 414–416.

Amsler, M., and Huber, A. (1946). Methodik und erste klinische Ergebnisse einer Funktionsprüfung der Blut-Kammerwasser-Schranke. *Ophthalmologica*, **111**, 155–176.

Amsler, M., and Verrey, F. (1946). Hétérochromie de Fuchs et fragilité vasculaire. *Ophthalmologica*, **111**, 178–181.

Campinchi, R. (1973). Fuchs' heterochromic uveitis. In *Uveitis, Immunological and Allergic Phenomena*, pp. 586–597. Editors: R. Campinchi, J. P. Faure, E. Bloch-Michel, and J. Haut. Thomas: Springfield.

Duke-Elder, S., and Perkins, E. S. (1966). Diseases of the uveal tract. In *System of Ophthalmology*, Vol. IX, pp. 594–602. Editor: S. Duke-Elder. Kimpton: London.

Ehinger, B., and Falck, B. (1966). Concomitant adrenergic and parasympathetic fibres in the rat iris. *Acta Physiologica Scandinavica*, **67**, 201–207.

Fuchs, E. (1906). Ueber Komplikationen der Heterochromie. *Zeitschrift für Augenheilkunde*, **15**, 191–212.

Georgiades, G. (1964). Les lésions de l'iris hétérochromique en général. *Bulletins et mémoires de la Société Française d'Ophthalmologie*, **77**, 465–487.

Helve, J., and Nieminen, H. (1974). Simultaneous bilateral fluorescein angiography of the anterior eye. *Acta Ophthalmologica*, Supplementum, **123**, 134–135.

Loewenfeld, I. E., and Thompson, H. S. (1973). Fuchs's heterochromic cyclitis: a critical review of the literature. I. Clinical characteristics of the syndrome. *Survey of Ophthalmology*, **17**, 394–457.

Perry, H. D., Yanoff, M., and Scheie, H. G. (1975). Rubeosis in Fuchs heterochromic iridocyclitis. *Archives of Ophthalmology*, **93**, 337–339.

Saari, M., Vuorre, I., and Nieminen, H. (1978). Infra-red transillumination stereophotography of the iris in Fuchs's heterochromic cyclitis. *British Journal of Ophthalmology*, **62**, 110–115.

Vassileva, P., Kottow, M., and Weigelin, E. (1975). Provoked iris ischaemia in the rabbit. I. Clinical and histopathological examinations. *Albrecht von Graefes Archiv für klinische und experimentele Ophthalmologie*, **196**, 231–238.

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Immunological investigations in post-traumatic granulomatous and non-granulomatous uveitis

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SUMMARY Histopathological and immunological investigations have been performed in 16 cases of post-traumatic granulomatous (10) and non-granulomatous uveitis (6). Most cases of sympathetic ophthalmitis showed evidence of cell mediated immunity to uveoretinal antigens, though it was not possible to make a definitive diagnosis on immunological grounds alone. Three patients with post-traumatic non-granulomatous uveitis showed a positive immunological response to ocular antigens, and 2 of these later developed clinical evidence of sympathetic ophthalmitis, which suggests that post-traumatic non-granulomatous uveitis in such cases may represent a presympathetic (i.e., incipient) or modified stage of the disease.

Perforating wounds of the eye are common and occur particularly in children at play or adults engaged in industry. Road traffic accidents also cause many. These ocular injuries show a wide variation in their clinical and histological behaviour. Thus, from minimal clinical signs and symptoms, the injured eyes may show laceration, disorganisation, purulent infection, prolapse of intraocular contents, chronic endophthalmitis, and phthisis bulbi. Occasionally the inflammation in the injured eye may take a different course, persisting for a long time; later the uninjured contralateral eye may show evidence of irritation and inflammation (i.e., sympathetic ophthalmitis), which may lead to blindness.

Although Hippocrates (459–355 BC) knew that persons who had lost one eye from injury frequently became blind in the other eye, William MacKenzie (1840), a clergyman who became an ophthalmologist, first fully documented this condition of sympathetic involvement of the uninjured eye. Fuchs (1905), however, first clearly described the histological changes in the injured (i.e., exciting) and the uninjured (i.e., sympathising) eyes. The subject was later extensively reviewed by Lowenstein (1945).

It is now generally agreed that in sympathetic ophthalmitis there is typically a diffuse and often massive infiltration of the entire uvea by lymphocytes and eosinophils, with foci of epithelioid cells frequently containing giant cells but without caseation. In the early stages the epithelioid cell nests are either absent or tend to be small (Collins, 1949), but later they increase in size, phagocytose melanin pigment, and merge with the lymphocytic infiltration, the result being a mottled appearance in the uvea (Figs. 1–4). Although the sensory retina is not affected by the infiltrate, isolated nodular lesions of epithelioid cells known as Dáleñ-Fuchs nodules may occur beneath the pigment epithelium, particularly in the region of the ciliary body and pars plana. A perforating wound, especially with uveal prolapse, is thought to be a constant feature in the exciting eye.

Because of the increased awareness of this complication and the wide usage of antibiotics and corticosteroids the incidence of typical sympathetic ophthalmitis appears to have fallen considerably, though there are still occasional reports of such complications even after sterile wounds such as are made in routine intraocular surgery (Shammas *et al.*, 1977). It is possible, however, that this apparent decrease in incidence may be due to the failure of clinical and histological diagnosis, at least in some unilateral cases, either because of early enucleation before the characteristic histological changes have appeared, or because the tissue response has been substantially modified by better wound repair and possible concomitant steroid therapy.

It has been shown that antigen-antibody aggregates prepared with different concentrations of the

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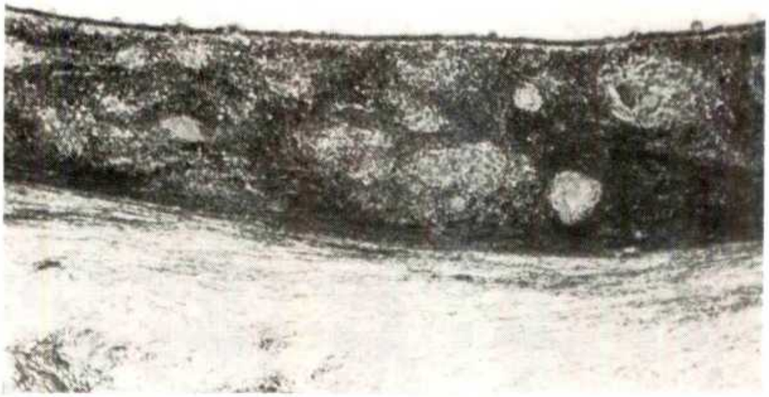

Fig. 1 *The typical mottled appearance in the uvea. The pale areas are foci of histiocytes and the dark areas represent lymphocytes and other inflammatory cells. Haematoxylin and eosin,* × 340

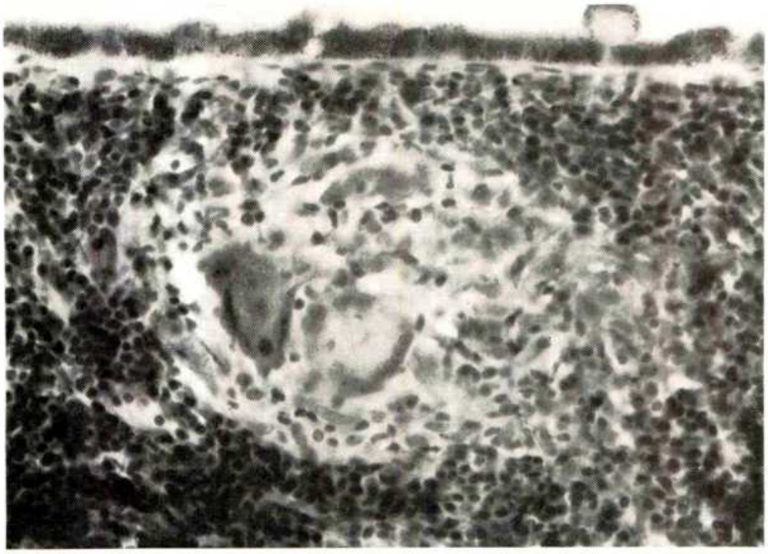

Fig. 2 *A focus of histiocytes and giant cells. Haematoxylin and eosin,* × 580

same antigen may produce different histological pictures, ranging from a simple leucocytic infiltration to well formed granulomata with typical epithelioid cells and giant cells (Spector and Heesom, 1969), and that the use of corticosteroids may modify or suppress the development of an allergic reaction. By analogy it is possible to expect a variation in the clinical and histological appearances of sympathetic ophthalmitis, which is considered to be an autoimmune disease due to sensitisation with uveoretinal antigens (Elschnig, 1910; Woods, 1921; Verhoeff, 1927; Friedenwald, 1934; Hammer, 1971; Marak, 1976) in which autosensitisation would depend on the nature of the injury—and therefore the amount of antigen released—and on the immune status of the individual.

It would also seem that the term sympathetic ophthalmitis may have a somewhat different connotation from clinical, histopathological, and immunological points of view. Thus to the clinician's sympathetic ophthalmitis is by definition bilateral uveitis in which inflammation in the injured eye is followed by inflammation in the uninjured eye. From the pathologist's point of view sympathetic ophthalmitis will be diagnosed only if there is the characteristic histological picture described above. If an injured eye shows only non-granulomatous inflammation, therefore, a pathologist will be reluctant to diagnose sympathetic ophthalmitis even if there is a clinical suggestion of some inflammation in the opposite uninjured eye. From the immunological point of view sympathetic ophthalmitis is an autoallergic phenomenon triggered by trauma and perhaps some occult infection in the injured eye, in which process the fellow eye may or may not be involved. Whether it is depends on the dose of

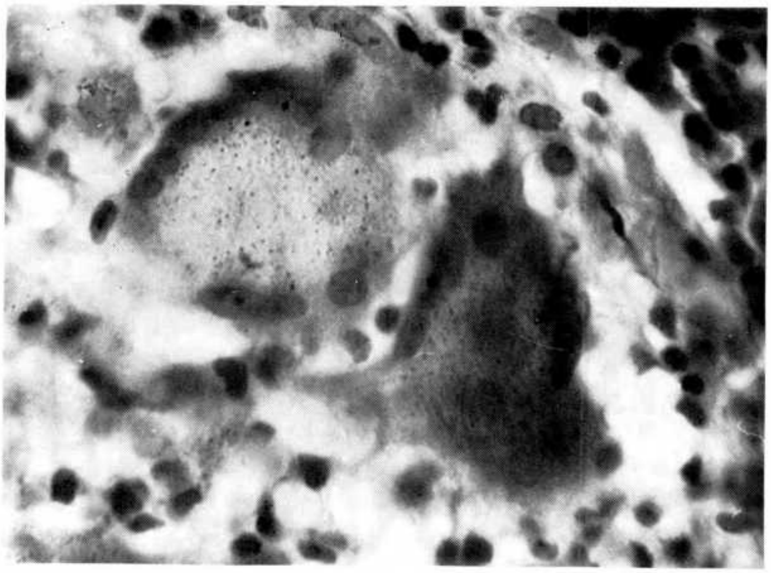

Fig. 3 *Two giant cells, containing melanin pigment within their cytoplasm. Haematoxylin and eosin,* ×1550

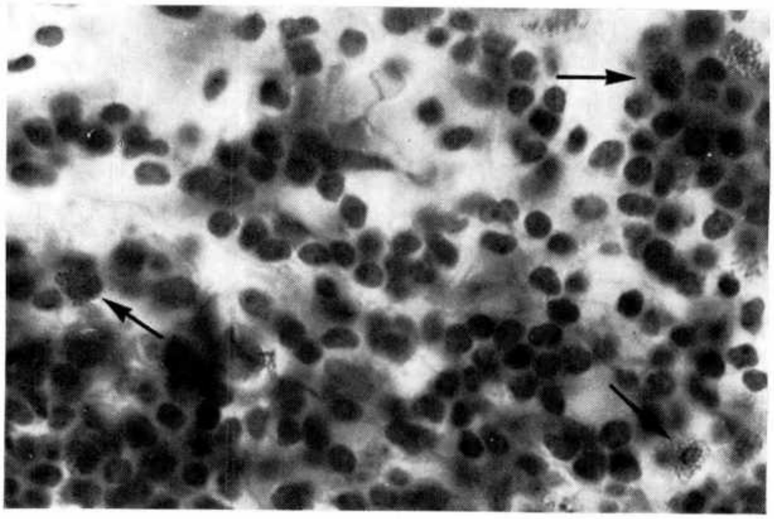

Fig. 4 *Lymphocytic infiltration of the choroid with 3 eosinophils (arrowed). Haematoxylin and eosin,* ×1550

the antigen, the way it is presented to the immunocompetent cells, the immune status of the individual, and whether or not he is being treated with immunosuppressive drugs. So long as these patients show in-vitro evidence of sensitisation to uveoretinal antigens, the immunologist can recognise the incipient or threatening stages of post-traumatic autoallergic uveitis (i.e., sympathetic ophthalmitis) whether the enucleated eye shows uveitis with the diagnostic histological features or not.

The question arises, therefore, whether a diagnosis of sympathetic ophthalmitis (post-traumatic allergic uveitis) can be entertained on the basis of positive immunological tests even if the uninjured eye is clinically normal at the time of investigation and the injured eye shows only the pathological changes of a nondescript inflammation (Fig. 5). The present study was carried out in an attempt to provide an answer to this question.

Methods and materials

A total of 16 patients were investigated. Fifteen of them had their injured eyes enucleated either because of early involvement of the other eye or because the injured eye was severely inflamed and painful and did not serve any useful purpose. The eyes were examined histologically by the conven-

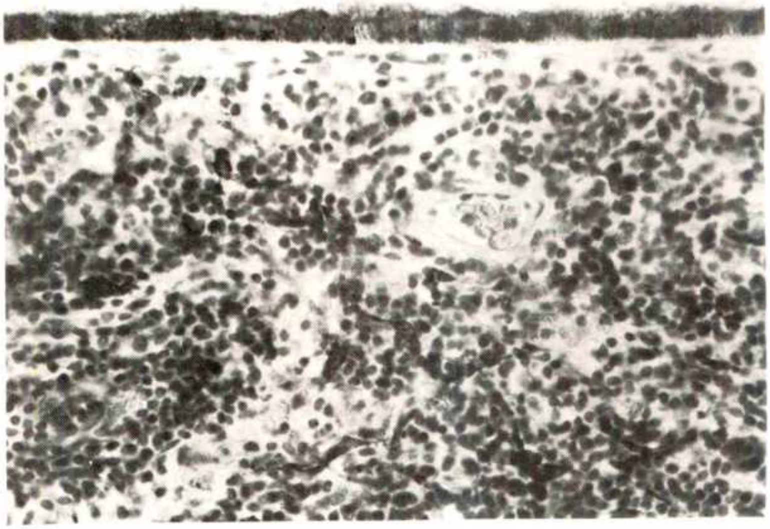

Fig. 5 *Non-granulomatous uveitis. Haematoxylin and eosin,* ×620

tional techniques (Ashton, 1967). In none of the eyes was there any evidence of lens-induced uveitis.

Blood was collected from these 15 patients either before or a few days after enucleation and examined for the serum concentrations of immunoglobulins G, A, and M by the standard radial immunodiffusion technique. Blood was also examined from 1 patient who showed clinical evidence of sympathetic ophthalmitis in the uninjured eye but in whom the histology of the eye was not available because the enucleation of the exciting eye was deferred.

Specimens of blood from 98 healthy adults matched for age and sex were also tested to obtain a normal range for the serum immunoglobulins. The individual values obtained were logarithmically transformed to obtain the mean and the range with 95% confidence limits. The significance of the differences between the means was tested by Student's *t* test.

Cryostat sections of a composite block consisting of rat liver, kidney, stomach, diaphragm, and parotid gland were used to detect non-organ-specific autoantibodies such as antinuclear, anti-smooth-muscle, antireticulin, antimitochondrial, and antiskeletal antibodies. A standard indirect immunofluorescent technique and an epifluorescence microscope (Zeiss) with FITC interference filter were used. The results were analysed by the chi-square method.

Delayed hypersensitivity (i.e., cellular immunity) to non-specific mitogens (e.g., phytohaemagglutinin) and to uveoretinal antigens was tested in 16 patients. The technique used was either the leucocyte migration inhibition test or the lymphocyte transformation test (Hammer, 1971, 1974). The antigens used in the present study were crude extracts of human choroid and the adherent retinal pigment epithelium, the sensory retina, and the anterior uvea. The various antigens were prepared as 10% (wet weight) homogenates in phosphate—buffered saline (pH 7·2), and 0·1 ml samples were used separately in each culture chamber or tube. The tests were duplicated, and a migration inhibition of more than 25% and a transformation index of over 1·5 were regarded as positive for the present study.

Results

HISTOPATHOLOGY

Of the 15 enucleated eyes 5 showed the typical features of granulomatous uveitis with Dálen-Fuchs nodules, and the contralateral eyes showed the clinical features of sympathetic ophthalmitis. In addition to these 5 cases 1 case showed the clinical features of sympathetic ophthalmitis with the ophthalmoscopic changes resembling Dálen-Fuchs spots (i.e., the clinical equivalent of histological nodules) in the exciting eye. This eye was not enucleated.

Ten enucleated eyes showed the histological features of non-granulomatous inflammation, but only in 2 cases did the contralateral eye show clinical evidence of mild inflammation initially, both these cases developing clear clinical signs of sympathetic ophthalmitis at a later date.

SERUM IMMUNOGLOBULINS

The results are summarised in Table 1 and the graph in Fig. 6. The geometric means of IgG and IgA levels were not significantly raised in either group

Table 1 *Serum immunoglobulins in post-traumatic uveitis*

Presenting diagnosis	*Number of cases*	*IgG IU/ml Mean (Range)*	*IgA IU/ml Mean (Range)*	*IgM IU/ml Mean (Range)*
Healthy adults	98	121 (68–217)	125 (55–286)	151 (68–333)
Granulomatous uveitis (sympathetic ophthalmitis)	6[*]	122 (80–210)	137 (99–210)	239[‡]
Non-granulomatous uveitis	10[†]	137 (100–178)	161 (99–312)	256[§] (140–480)

[*] One case diagnosed clinically but not histopathologically
[†] Two cases developed clinical evidence of sympathetic ophthalmitis at a later date
[‡] $P<0{\cdot}01$
[§] $P<0{\cdot}001$

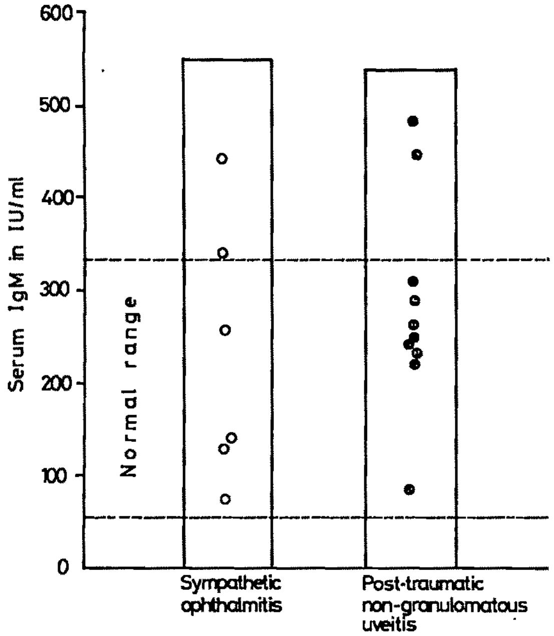

Fig. 6 *Serum immunoglobulin M in post-traumatic granulomatous and non-granulomatous uveitis*

of cases. Though the geometric mean concentration of IgM was raised in both groups, it will nevertheless be seen from the graph that only 2 cases each of sympathetic ophthalmitis and non-granulomatous uveitis showed levels which were above the upper limit of the normal range.

NON-ORGAN-SPECIFIC AUTOANTIBODIES

Smooth muscle antibodies in low titres (1/10) were present in the serum of 2 cases of sympathetic ophthalmitis and in 3 cases of non-granulomatous uveitis. Antinuclear antibodies were found in only 1 case of sympathetic ophthalmitis. The incidence of these non-organ-specific autoantibodies was statistically insignificant.

CELL MEDIATED IMMUNITY

The results are summarised in Table 2. Of the 6 cases of sympathetic ophthalmitis (5 histologically proved and 1 diagnosed clinically) 3, including the case diagnosed clinically, showed evidence of delayed tissue allergy to uveoretinal antigens (i.e., choroid + pigment epithelium). One case reacted against sensory retinal antigen and another against anterior uveal extract. The test was negative in 1 case in spite of both histological and clinical evidence of sympathetic ophthalmitis.

On the contrary, 7 of the 10 cases of post-traumatic non-granulomatous uveitis showed no evidence of delayed tissue allergy to uveoretinal antigens. In 2 of the 3 other cases with a positive lymphocyte transformation test, however, clinical evidence of sympathetic ophthalmitis developed several weeks later.

The response to non-specific mitogens (phytohaemagglutinin) was normal.

Discussion

It would appear that in a fully developed case of sympathetic ophthalmitis the enucleated eye generally shows features of granulomatous panuveitis with well developed Dälen-Fuchs nodules. Occasionally, however, if the duration of onset is short and enucleation is performed at the first suspicion of sympathetic ophthalmitis (as happened in 1 of our cases) the eye may not show granulomatous

Table 2 *Cell-mediated immunity in post-traumatic uveitis (lymphocyte transformation and leucocyte migration inhibition tests)*

Presenting diagnosis	*Number of cases*	*Number positive*			*Number negative*
		Choroid and retinal pigment epithelium	*Sensory retina*	*Anterior uvea*	
Granulomatous uveitis (sympathetic ophthalmitis)	6	3[*]	1	1	1
Non-granulomatous uveitis	10	3[†]	—	—	7

[*] One case diagnosed clinically but not histopathologically
[†] Two cases developed clinical evidence of sympathetic ophthalmitis at a later date

lesions (Greaves, 1948), either because there has been insufficient time for this reaction to develop or the immune response of the host was not congenial, or because the physicochemical nature of the antigen-antibody aggregate was such that it did not stimulate a granulomatous reaction (Spector and Heesom, 1969). In such doubtful cases immunological investigations concerning cellular immunity to uveoretinal antigens may be diagnostically helpful, although, as is evident from this study, these tests may be negative in a proportion of histologically proved cases of sympathetic ophthalmitis (see Table 2).

In the past it has been argued that the offending antigen in sympathetic ophthalmitis is the uveal pigment. The present study has demonstrated, however, that patients may show evidence of hypersensitivity to other antigens such as those residing in the photoreceptors and the pigment epithelium of the retina (Rahi, 1970; Reich *et al.*, 1974). Thus it provides further evidence to support the recognised view that sympathetic ophthalmitis is an autoimmune disease (Collins, 1949) involving both uveal and retinal antigens (Wong *et al.*, 1971; Marak *et al.*, 1971; Marak *et al.*, 1973).

The significance of a raised IgM in some cases of post-traumatic non-granulomatous uveitis is not known. Woods (1921), using bovine uvea as antigen, detected complement-fixing antibodies in those cases of post-traumatic uveitis which ultimately did not progress to classical sympathetic ophthalmitis. It is of interest that IgM is a complement-fixing antibody which, as suggested by Woods, may have a protective role, and this phenomenon may be analogous to immune enhancement in malignant tumours. This may not be true, however, in every case, because some of the patients with sympathetic ophthalmitis also had raised levels of IgM.

It is possible on the other hand that post-traumatic non-granulomatous uveitis represents a 'forme fruste' or an early stage of sympathetic ophthalmitis or allergic uveitis which, due to some unknown cause, remains limited to the injured eye. In some cases, as time progresses and the patients develop cellular hypersensitivity, the reaction becomes granulomatous and the other eye becomes involved. Thus the appearance of delayed tissue allergy to uveoretinal antigens after a penetrating wound of the eye in an otherwise healthy person may signify ocular hypersensitivity, and a well controlled study with a long follow-up could ultimately decide whether or not such individuals should be treated with immunosuppressive drugs at least during the period when the disease in the injured eye is active.

It has been suggested that sympathetic ophthalmitis may begin as 'traumatic uveitis serosa', possibly due to invasion by a virus (Sie-Boen-Lian, 1963) or to mycoplasma (Schrek, 1975), which may progress due to autosensitisation and involve the other eye to produce the histological changes typical of sympathetic ophthalmitis. In these cases raised IgM levels may represent an immune response to an occult or a subclinical intraocular infection. It may be of help, therefore, if all patients with perforating wounds have their immunological profile, in particular their cellular immune responses, investigated at reasonably frequent intervals until the inflammation subsides, so that corticosteroids and other immunosuppressive drugs may be given in sufficient doses at a time when they are most likely to be beneficial.

There was no increased incidence of non-organ-specific autoantibodies in sympathetic ophthalmitis, and the response to phytohaemagglutinin was normal. This supports the view that the T lymphocyte population is normal in this disease (Boone *et al.*, 1976), though the 'null' lymphocytes (i.e., lymphocytes which are neither B nor T) may be increased in some patients.

It was stated in the introduction to this paper that the purpose of the investigations was to see whether or not a diagnosis of sympathetic ophthalmitis can be made on the basis of positive immunological tests even if the uninjured eye is clinically normal at the time of investigation and the injured eye shows only the pathological changes of non-granulomatous inflammation. Since some cases of both sympathetic ophthalmitis and simple post-traumatic non-granulomatous uveitis showed raised IgM levels, this immunological criterion does not appear to have a diagnostic significance. On the other hand 5 of 6 cases of sympathetic ophthalmitis showed evidence of cell-mediated hypersensitivity to uveoretinal antigens, though 1 case which was confirmed histopathologically showed no evidence of a positive reaction, in spite of the fact that the immunological response had not been suppressed by steroid therapy. Seven of the 10 cases of post-traumatic non-granulomatous uveitis did not show positive cell-mediated immunological responses, though 2 of the 3 other cases with positive responses later developed clinical evidence of sympathetic ophthalmitis.

It is clear from these results that the cell-mediated immunological response to ocular antigens in both typical and atypical cases of sympathetic ophthalmitis is often positive, although it may sometimes be negative. Occasionally, however, some patients may never develop sympathetic ophthalmitis even in the presence of a positive cell-mediated hypersensitivity to uveoretinal antigen. It is not possible, therefore, to make a definitive diagnosis of sympathetic ophthalmitis on immunological grounds alone.

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References

Ashton, N. (1967). Techniques for the histological examination of the eye. *Association of Clinical Pathologists Broad Sheet* No. 59. BMA: London.

Boone, W. B., Gupta, S., Hanson, J., and Good, R. A. (1976). Lymphocyte subpopulation in patients with sympathetic ophthalmitis and non-granulomatous uveitis. *Investigative Ophthalmology*, **15**, 957–961.

Collins, R. C. (1949). Experimental studies on sympathetic ophthalmia. *American Journal of Ophthalmology*, **32**, 1687–1699.

Elschnig, A. (1910). Studien zur sympathischen Ophthalmie. *Albrecht von Graefes Archiv für Ophthalmologie*, **76**, 509–546.

Friedenwald, J. S. (1934). Notes on allergy theory of sympathetic ophthalmia. *American Journal of Ophthalmology*, **17**, 1008–1018.

Fuchs, E. (1905). Uber sympathisierende Entzündung. *Albrecht von Graefes Archiv für Ophthalmologie*, **61**, 365–456.

Greaves, A. (1948). A contribution to the microscopical anatomy of the sympathizing eye. *British Journal of Ophthalmology*, **32**, 545–550.

Hammer, H. (1971). Lymphocyte transformation test in sympathetic ophthalmitis and the Vogt-Koyanagi-Harada syndrome. *British Journal of Ophthalmology*, **55**, 850–852.

Hammer, H. (1974). Cellular hypersensitivity to uveal pigment confirmed by leucocyte migration tests in sympathetic ophthalmitis and the Vogt-Koyanagi-Harada syndrome. *British Journal of Ophthalmology*, **58**, 773–776.

Hippocrates (459–355 BC). Quoted by Samuels, B., and Fuchs, A. (1952). *Clinical Pathology of the Eye*, pp. 148–164. Cassell: Toronto.

Lowenstein, A., (1945). The sympathizing eye. Transactions of the *Ophthalmological Societies of the United Kingdom*, **65**, 219–231.

Mackenzie, W. (1840). *A Practical Treatise on the Diseases of the Eye*, 3rd edn., pp. 523–534. Longman: London.

Marak, G. E. (1976). Immunopathology of sympathetic ophthalmia. *Modern Problems in Ophthalmology*, **16**, 102–105.

Marak, G. E., Aye, M. S., and Alepa, F. B. (1973). Cellular hypersensitivity in penetrating eye injuries. *Investigative Ophthalmology*, **12**, 380–382.

Marak, G. E., Font, R. L., Johnson, M. C., and Alepa, F. P. (1971). Lymphocyte-stimulating activity of ocular tissues in sympathetic ophthalmia. *Investigative Ophthalmology*, **10**, 770–774.

Rahi, A. H. S. (1970). Autoimmunity and the retina. *British Journal of Ophthalmology*, **54**, 441–444.

Reich D'Almeida, F., and Rahi, A. H. S. (1974). Antigenic specificity of retinal pigment epithelium and non-immunological involvement in retinal dystrophy. *Nature*, **252**, 307–308.

Schrek, E. (1975). Further investigations for the demonstration of a specific microorganism in sympathetic ophthalmia. *Albrecht von Graefes Archiv für klinische und experimentelle Ophthalmologie*, **193**, 229–243.

Shammas, H. F., Zubyk, N. A., and Stanfield, T. F. (1977). Sympathetic uveitis following glaucoma surgery. *Archives of Ophthalmology*, **95**, 638–641.

Sie-Boen-Lian (1963). Cultivation of virus in a case of sympathetic ophthalmia. *Ophthalmologica*, **146**, 43–47.

Spector, W. G., and Heesom, N. (1969). The production of granulomata by antigen-antibody complexes. *Journal of Pathology*, **98**, 37–39.

Verhoeff, F. H. (1927). An effective treatment for sympathetic uveitis. *Archives of Ophthalmology*, **56**, 28–41.

Wong, V. G., Anderson, R., and O'Brien, P. J. (1971). Sympathetic ophthalmia and lymphocyte transformation. *American Journal of Ophthalmology*, **72**, 960–968.

Woods, A. C. (1921). Immune reactions following injuries to the uveal tract. *Journal of the American Medical Association*, **77**, 1317–1322.

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Streptococcus suis type II (group R) as a cause of endophthalmitis

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SUMMARY A case is reported of a patient with bilateral endophthalmitis, meningitis, sensorineural deafness, labyrinthitis, and septicaemia due to *Streptococcus suis* type II (group R). The organism is known to produce epidemic meningitis, septicaemia, and purulent arthritis in piglets, but human infection is rare, and no other case reports of ocular infection are known. The organism was sensitive to penicillin at a minimum inhibitory concentration of 0·03 mg/l.

Streptococcus suis type II is a recognised cause of epidemic infection in piglets, causing meningitis, septicaemia, and purulent arthritis (Field *et al.*, 1954; de Moor, 1963; Elliott, 1966). Human infection occurs rarely and is usually in people whose work involves prolonged contact with live or slaughtered pigs (Zanen and Engel, 1975). Case reports of human disease comprising septicaemia and meningitis have appeared from Denmark (Perch *et al.*, 1968; Koldkjaer and Nielsen, 1971), Holland (Zanen and Engel, 1975), and Great Britain (Hickling and Cormack, 1976).

In the case reported here the patient had, in addition to a septicaemia and meningitis, a sensorineural deafness, labyrinthitis, and severe bilateral endophthalmitis. This is the first report of endophthalmitis secondary to *Streptococcus suis* type II (group R).

Case report

A 46-year-old Caucasian man who worked as a maintenance engineer at a pork pie factory was well until 18 November 1976, when he complained of malaise and shivering. Over the succeeding 4 days he developed deafness in the right ear and ringing in both ears, unsteadiness of gait, vomiting, sleeplessness, and irritability. The eyes became watery. A headache developed and the malaise increased. Two days before admission to hospital the left vision deteriorated, and 1 day before admission the eyes became sticky. His general practitioner noted a hazy left cornea and a fixed dilated left pupil in addition to neck stiffness and referred the patient with a diagnosis of either meningitis or encephalitis.

On admission to the Oxford Eye Hospital on 23 October 1976 the patient was obtunded and his complaints were as described above. He made no complaint of ocular pain or discomfort but mentioned some wrist pain. Systemic examination showed dehydration, purulent pharyngitis, tender swollen wrists, unsteadiness, and a temperature of 37·6°C. The patient was lethargic but responsive to questioning. At this time he had no neck stiffness. Bilateral eighth nerve deafness (worse on the right) and labyrinthitis were noted. No skin lesions were identified, though one observer later noted transient petechiae at the elbows.

Ophthalmic examination showed a visual acuity of 6/9 on the right and hand movements on the left without correction. The intraocular pressures were right 36 mmHg and left 38 mmHg. There was bilateral diffuse conjunctival and episcleral injection, and conjunctival haemorrhages were present on the left. In addition there was a haemorrhagic papillary reaction in the upper tarsal conjunctiva. A purulent discharge was present in the left conjunctival sac. The right cornea showed diffuse vesicular epithelial oedema (bedewing) with mild stromal oedema and Descemet's folds. A marked cellular response in the anterior chamber resulted in a red reflex with no fundus view. The pupil was small, round, and reacted sluggishly. The left cornea showed diffuse epithelial and stromal oedema of moderate degree with circumferential infiltration in the paralimbal zone for 360°. Stromal folds were observed. The posterior corneal surface had large curdy precipitates. A deep anterior chamber showed a marked

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flare and cells and a 2 mm hypopyon. The pupil was fixed in mid-dilation, with no red reflex and no view of the fundus.

A diagnosis of bilateral endophthalmitis with secondary glaucoma, left purulent conjunctivitis, and toxic labyrinthitis with sensorineural deafness was made. Subsequent findings confirmed further diagnoses of meningitis and septicaemia.

LABORATORY FINDINGS

Bilateral nasal swabs gave no growth, and the conjunctiva grew only *Staphylococcus albus*. Cytology showed a large number of leucocytes in the left conjunctival smear and a few in the right. The turbid cerebrospinal fluid revealed a pleomorphic cellular picture (polymorphs 331/mm, lymphocytes 29/mm)) and protein 0·8 g/litre. Gram-positive cocci were observed in pairs and short chains.

A left anterior chamber tap showed similar Gram-positive cocci. Cultures of the cerebrospinal fluid, aqueous, and blood grew a β-haemolytic streptococcus which gave a weak reaction with Lancefield group D antiserum (after both acid extraction and autoclaving) but was not resistant to bile. An initial identification of the organism was *Streptococcus faecalis*. However, the organism was examined by the Streptococcus Reference Laboratory, Colindale, and by Dr S. D. Elliott, Cambridge, and was identified as *Streptococcus suis* type II. The minimum inhibitory concentration of penicillin and ampicillin was 0·03 mg/l. Haematological investigations included, haemaglobin 14·5 g/decilitre; haematocrit 44·3 g/dl, white blood count $8{\cdot}1\times10^9$/l (polymorphs 84%, lymphocytes 14%, monocytes 2%), and erythrocyte sedimentation rate 94 mm in the first hour.

TREATMENT

Initial therapy included benzylpenicillin 4 megaunits 4-hourly intravenously, prednisolone 80 mg daily, probenecid 500 mg 8-hourly, and acetozolamide 250 mg 6-hourly. In addition the patient received bilateral topical bacitracin drops (5000 units/ml) 4 times daily, dexamethasone (Maxidex) drops 0·1% hourly, atropine drops 1% twice daily, and subconjunctival benzylpenicillin 500 000 units, betamethasone (Betnesol) 4 mg, and Mydricaine 0·3 ml. The patient also received benzylpenicillin 20 000 units intraathecally as a stat dose.

After 2 days sytemic antibiotic therapy was changed to ampicillin 1 g 4-hourly, and subconjunctival ampicillin 100 mg was substituted for crystalline penicillin. The patient received subconjunctival ampicillin and betamethasone on alternate days to each eye. Systemic antibiotic therapy continued for 6 weeks.

PROGRESS

The patient developed a pyrexia which slowly returned to normal with the systemic therapy. The right cornea also cleared, and despite the anterior uveitis no vitreous reaction occurred at any time. The left cornea also cleared, but an increasing hypopyon developed after 1 week of therapy despite a resolution of other signs of inflammation. The hypopyon showed a curious tan colour. Ocular pressures returned to normal in the right eye within 24 hours but remained a persistent problem in the left eye, with readings in the mid 20s.

An intumescent cataract and pupillary block glaucoma developed as a late complication in the left eye. Extensive iridocapsular adhesions necessitated a left extracapsular lens extraction and broad iridectomy. Postoperatively a thick cyclitic membrane was seen behind the lens capsule. A hazy fundus view at this time showed no focal inflammatory lesions. A persistent postoperative flat chamber due to pupillary block resulted in bullous keratopathy and secondary glaucoma in this eye. At the time of writing the right eye remains entirely normal, with uncorrected vision of 6/5 and intraocular pressure of 16 mmHg.

The permanent auditory deficits include no vestibular function on either side. A cold caloric test showed no response from either ear. On the right a severe sensorineural deafness thought to be cochlear or retrocochlear has persisted. On the left a 20 to 30 decibel loss is detected. However, the patient shows good speech discrimination. Although not an auditory cripple, he continues to have balancing problems owing to his total loss of vestibular function.

Discussion

Previous case reports of *Streptococcus suis* type II infections in man have described septicaemia and meningitis. Only one earlier human case has shown joint involvement (Hickling and Cormack, 1976). Deafness and vestibular disturbance appear to be the commonest permanent sequelae. In one report left and right sided nystagmus occurred (Zanen and Engel, 1975). Previous reports have not mentioned endophthalmitis or conjunctivitis in man. In 1 report of porcine disease the infected pig appeared to have poor vision (Field *et al.*, 1954).

The origin of infection in piglets is probably the nasopharynx. Some human infections are probably associated with wound infection. It is of interest in the case reported here that a purulent pharyngitis was present. Although the possibility exists that the eyes might have been the site of entry via the conjunctival sac, the sequence of events suggests that a septicaemia, as shown by shivering and malaise, predated the ocular symptoms. This would be in keeping with the endophthalmitis being metastatic in origin rather than due to exogenous infection (Shammas, 1977). Metastatic endophthalmitis commonly presents painlessly, with the first ocular symptoms being visual. The reason for this remains obscure, and the lack of pain contrasts with the severity of the uveal inflammation. However, other authors (Walker and Fenwick, 1962) have noted this finding. The possibility must also be considered that the conjunctivitis was metastatic, though it is more likely that it arose from direct inoculation of the organism into the conjunctival sac.

The patient worked as a maintenance man in a pork pie factory. One of his assignments was to alter the operation of the various processing machines when a different type of pie was programmed. This involved priming the machines with raw meat, which gave ample opportunity for contact. The history and clinical course, except for the endophthalmitis, are characteristic of reported infections secondary to *Streptococcus suis* type II (group R).

This organism appears to be an occupational hazard for people working with raw pig meat. Nine of the 10 human cases reported by Zanen and Engel (1975) worked in close extended contact with live or slaughtered pigs. Of these 10 patients who had purulent meningitis with positive cerebrospinal fluid cultures 5 showed positive blood cultures and 5 showed decreased hearing. The case presented here is the first reported with endophthalmitis.

We acknowledge the help of Dr S. D. Elliott, Department of Pathology, University of Cambridge, and Dr W. R. Maxted, Cross Infection Reference Laboratory, Colindale, for identifying *Streptococcus suis* Type II. Thanks are due to Mr A. Freeland for the otological assessment.

References

Elliott, S. D. (1966). Streptococcal infection in young pigs. *Journal of Hygiene*, **64**, 205–212.

Field, H. I., Buntain, D., and Done, J. T. (1954). Studies on piglet mortality I. Streptococcal meningitis and arthritis. *Veterinary Record*, **66**, 453–455.

Hickling, P., and Cormack, F. C. V. (1976). Meningitis caused by group R haemolytic streptococci. *British Medical Journal*, **4**, 1299–1300.

Koldkjaer, O., and Nielsen, G. (1972). Haemolytic streptococcus group R infection. *British Medical Journal*, **3**, 765.

Moor, C. E. de (1963). Septicaemic infection in pigs caused by haemolytic streptococci of new Lancefield groups designated R, S, and T. *Antonie van Leeuwenhoek, Journal of Microbiology and Serology*, **29**, 272–280.

Perch, B., Kristjansen, P., and Skadhange, K. (1968). Group R streptococcus pathogenic for man. *Acta Pathologica et Microbiologica Scandinavica*, **74**, 69–76.

Shammas, H. F. (1977). Endogenous E. coli endophthalmitis. *Survey of Ophthalmology*, **21**, 429–435.

Walker, C. B., and Fenwick, P. (1962). Bilateral fulminating endophthalmitis with streptococcal septicaemia. *British Journal of Ophthalmology*, **46**, 281–284.

Zanen, H. C., and Engel, H. W. B. (1975). Porcine streptococcus causing meningitis and septicaemia in man. *Lancet*, **1**, 1286–1288.

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Canaliculitis with isolation of *Pityrosporum pachydermatis*

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SUMMARY A case of canaliculitis with obstruction of the lacrimal canaliculus and accumulation of conglomerates is described. *Pityrosporum pachydermatis* was cultured from the conglomerates. To the best of our knowledge this organism has not been previously implicated in such infections. Cure was obtained by treatment with nystatin administered topically and as an irrigation of the lacrimal pathways. The possibility that the pathogenesis of the canaliculitis and obstruction of the lacrimal pathways lies in decreased function of the lacrimal pump is discussed.

Canaliculitis is a well known clinical entity despite its relative rarity (Vaughan *et al.*, 1965). Various organisms have been described in its aetiology, including bacteria, actinomycetes, and fungi (Donahue, 1949; Vaughan *et al.*, 1965; Francois, 1968; Locatcher-Khorazo and Seegal, 1972; Duke-Elder, 1974). The fungi have included *Aspergillus*, *Candida*, *Trichosporon*, *Scopulariopsis*, and *Cephalosporium* species (Francois, 1968; Locatcher-Khorazo and Seegal, 1972). The present work describes a case of a complete occlusion of the lacrimal canaliculus due to a deposit of concrement from which *Pityrosporum pachydermatis* was cultured. To the best of our knowledge this species of fungus has not been previously implicated in such infections.

Case report

A 61-year-old man suffered for a year with irritation, redness, production of tears, and a yellow secretion of pus from the left eye. He was treated topically with different corticosteroid and antibiotic drugs without improvement. The purulent secretion increased, and he was referred to our outpatient clinic with a tentative diagnosis of dacryocystitis and/or infected chalazion. Examination of the left eye showed a swelling of the inner part of the lower lid and a button of yellow secretion in the lacrimal punctum (Fig. 1). There was a symblepharon of the conjunctiva connecting the margin of the lacrimal punctum with the plica, with traction on the punctum. Throughout the examination a continuous epiphora was observed.

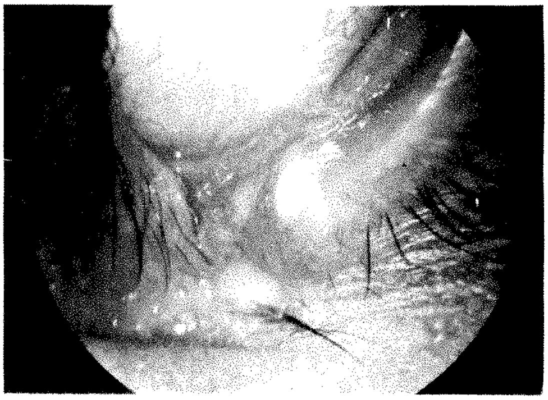

Fig. 1 *Button of yellow purulent secretion on the lacrimal punctum*

The lacrimal pathways of both eyes were rinsed with saline, which passed freely to the pharynx, raising the suspicion of a canalicular infection. Conglomerates of yellow material (Fig. 2) were obtained by pressure with the finger on the area of the lacrimal duct in the direction of the canaliculus and lacrimal punctum. This material was cultured for bacterial and fungal agents. These cultures yielded Gram-positive micrococci and a yeast-like

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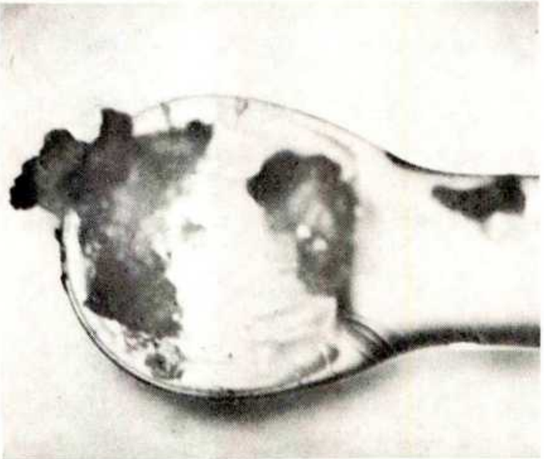

Fig. 2 *Conglomerates of yellow material pressed out from the canaliculus*

organism growing on Sabouraud's dextrose agar (Figs. 3 and 4) both at room temperature and at 37°C. The microscopic examination of subcultures from cornmeal agar revealed the presence of blastospores with mycelium.

Tests of assimilation of glucose, maltose, sucrose, lactose, galactose, xylose, trehalose, raffinose inositol melibiose, and cellobiose using the classical Wickerham method (Lodder, 1971) were negative. A weak assimilation of glucose was seen by an auxinographic technique (Huppert *et al.,* 1975; Segal and Ajello, 1976). Fermentation of glucose, maltose, sucrose, and lactose and the urease test gave negative results. Applying an auxinographic method for nitrogen compounds assimilation revealed the assimilation of ammonium sulphate and not of potassium nitrate. These various morphological and biochemical characteristics were confirmed by the Fungus Diagnostic Branch of the Mycology Division at the Center for Disease Control in Atlanta, Georgia, USA, where the organism was identified as *Pityrosporum pachydermatis.*

Treatment was initiated with the antifungal agent nystatin, administered as drops (7000 units nystatin/ml saline), 2 drops 6 times a day for a month, and as an irrigation of the lacrimal pathways twice a week. In addition, the symblepharon was released. After a month of this treatment a cure was obtained.

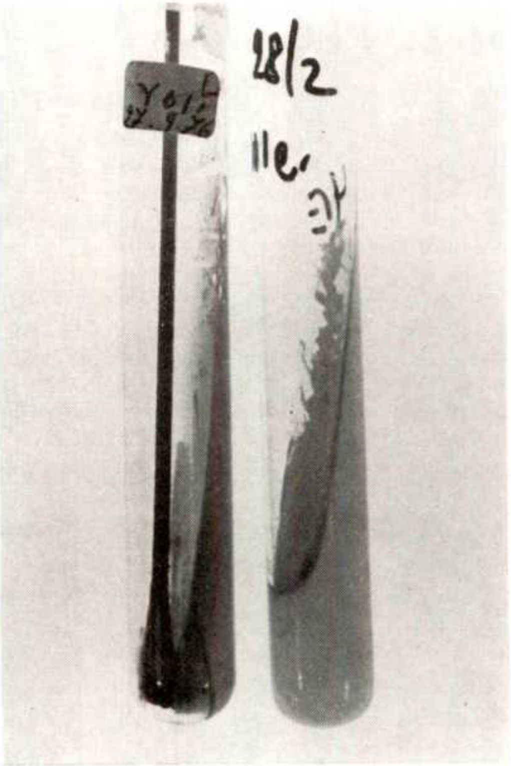

Fig. 3 *Yeast-like culture isolated from conglomerates*

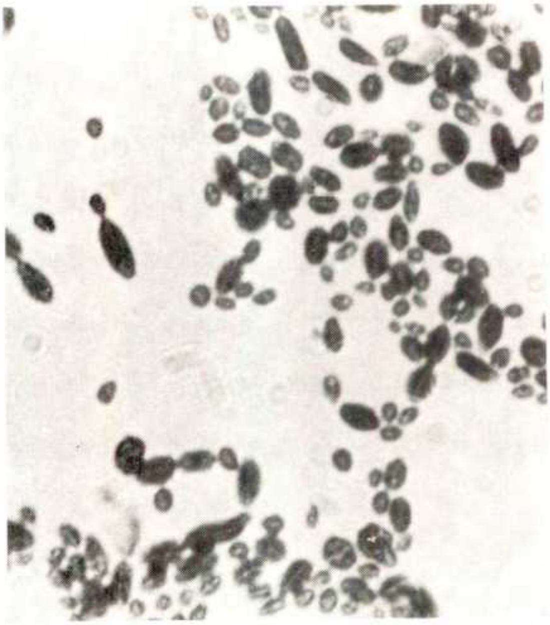

Fig. 4 *Budding yeast cells from Sabouraud's dextrose agar culture*

Discussion

Accumulation of material in the form of conglomerates is found in canaliculitis due to actinomyces (Francois, 1968). Wolter and Deitz (1963) described a case of dacryocystitis due to *Candida albicans* with concrement formation in the lacrimal sac. The isolation of *Pityrosporum pachydermatis* from the conglomerates in the canaliculus of our case raises the possibility that conglomerate formation may be a more general phenomenon in microbial canaliculitis.

Pityrosporum species (*P. orbiculare* and/or *P. ovale*) have been associated with ocular disease, specifically seborrhoeic blepharitis, although there is no definite proof of their aetiological role in these diseases (Parunovic and Halde, 1967; Francois, 1968; Locatcher-Khorazo and Seegal, 1972). The isolation of *P. pachydermatis* from the conglomerates in our case, and the cure following treatment with a specific antifungal substance, point to the involvement of this organism in the ocular infection.

We wish to express our appreciation to the staff of the Fungus Diagnostic Branch, Mycology Division, Center for Disease Control, Atlanta, and Professor D. Ahearn, Department of Biology, Georgia State University, Atlanta, Georgia, USA, for their assistance in identification of the organism and valuable information.

References

Donahue, H. C. (1949). Unusual mycotic infection of the lacrimal canaliculi and conjunctiva. *American Journal of Ophthalmology*, 32, 207–210.

Duke-Elder, S. (1974). *System of Ophthalmology*, vol. 13, pp. 693–698. Henry Kimpton: London.

Francois, J. (1968). *Les Mycoses Oculaires*, pp. 42–49, 139, Masson: Paris.

Huppert, M., Harper, G., Sung, S. H., and De Lanerolle, V. (1975). Rapid methods for identification of yeasts. *Journal of Clinical Microbiology*, 2, 21–34.

Locatcher-Khorazo, D., and Seegal, B. C. (1972). *Microbiology of the Eye*, pp. 72–73, 216–226. Mosby: St. Louis.

Lodder, J. (1971). *The Yeasts*, pp. 65–84. North Holland: Amsterdam.

Parunovic, A., and Halde, C. (1967). Pityrosporum orbiculare: its possible role in seborrheic blepharitis. *American Journal of Ophthalmology*, 63, 815–820.

Segal, E., and Ajello, L. (1976). Evaluation of a new system for the rapid identification of clinically important yeasts. *Journal of Clinical Microbiology*, 4, 157–159.

Vaughan, D., Cook, R., and Asbury, T. (1965). *General Ophthalmology*, pp. 62–64. Lange Medical Publications: Los Altos.

Wolter, J. R., and Deitz, M. R. (1963). Candidiasis of the lacrimal sac. *American Journal of Ophthalmology*, 55, 153–155.

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Book reviews

Mikro-Chirurgie der Glaukome. By M. M. KRASNOV. 1977. Pp. 174, figs., tables, refs. George Thieme, Leipzig (49 DM)

This book gives the impression that it has been in press for about 10 years. It appears to deal with the microsurgery of glaucoma prevailing at the time of the Burgenstock microsurgery conference in 1968.

At present sinusotomy is being performed nowhere except perhaps in focal regions in the Soviet Union. Trabeculotomy for open-angle glaucoma has to all intents and purposes been abandoned even in West Germany. Trabeculectomy—here named Sektorensinusektomie—has replaced both procedures everywhere, including, by all accounts, the Soviet Union. The extensive literature on trabeculectomy has been completely ignored. Indeed, the grossly inadequate bibliography contains no references later than 1972, and many important references before this date are missing. For example, no credit has been given to Walker and Kanagasandram, whose external fistulisation of Schlemm's canal preceded sinusotomy, and is exactly the same procedure. The concept of canalicular blockage receives scant attention, and surgical procedures based on it—namely, goniospasis and laser coagulation of the peripheral iris—none at all. The illustrations are in general adequate, but it is sad that many of them have been reproduced without any acknowledgement of their source.

As a propaganda exercise this book may succeed in the Eastern bloc, but as an international contribution to the microsurgery of glaucoma it is inadequate. J. E. CAIRNS

Vitreous Surgery and Advances in Fundus Diagnosis and Treatment. Edited by H. MACKENZIE FREEMAN, TATSUO HIROSE, and CHARLES L. SCHEPENS. 1977. Pp. 681, figs., tables, refs. Appleton-Century-Crofts, New York (£50)

This is one of the best of several recent publications on vitreoretinal disorders. It presents the proceedings of the Vitreoretinal Congress which was held in Boston in June 1975.

The text is divided into two main parts. The first, and by far the largest part, deals with the vitreous. It begins with a detailed description of the normal and abnormal vitreous. The short chapter by Constable on vitreous membranes is particularly interesting. The second section deals with methods of examination of the vitreous, with detailed descriptions of ultrasonography and the evaluation of retinal function in the presence of vitreous opacities. The last chapter in this section, on the preoperative medical evaluation of patients undergoing vitrectomy, written by a physician, is particularly important. By far the largest section is devoted to closed vitreous surgery. It deals with observation and illumination during surgery and detailed descriptions of all the vitrectomy instruments by their designers. The many chapters on surgical techniques are of particular interest. They include vitrectomy techniques and results in diabetes, trauma, and complicated retinal detachments. The section on vitreous injections describes the use of intravitreal gas injections and vitreous substitutes. It is interesting to note that liquid silicone is mentioned only very briefly. The last section, written mainly by the Boston group, deals with open-sky vitrectomy.

The second part of the book deals with the retinal and choroidal circulation and the use of monochromatic light in the diagnosis and treatment of retinal disorders.

This book is highly recommended to readers interested in vitreoretinal surgery. Most of the chapters are short and very readable, with excellent illustrations. The discussions that follow most of them are particularly informative. J. J. KANSKI

Optics in Vision. By HENRI OBSTFELD. 1978. Pp. 327, figs., tables, refs. Butterworths, London (£10·50)

This useful book covers the subject of ocular optics adequately. To be precise, the question of vision does not enter the problem except when subjective refraction comes to the aid of objective methods. The term 'visual optics' covers a larger field not encompassed by this book.

The text leans heavily on old friends, well-known diagrams having been lucidly redrawn and computational methods having passed through a clarifying sieve. On the rare occasions when the author strays into perceptual problems, such as perceived size, he slips up not on grounds of psychology but on those of physiology. The book illustrates the unfortunate situation generated by the SI system of units, metres and millimetres being mixed almost *ad lib*. A generation beginning to come to grips with the advantages of the decimal point could have been spared this unnecessary complication. However, the book covers all clinical needs, and its approach to contact lens optics is of more than a passing interest. R. A. WEALE

Symposium on Ocular Therapy. Vol. 10. Edited by IRVING M. LEOPOLD and ROBERT P. BURNS. 1977. Pp. 123, figs., tables, refs. John Wiley, Chichester (£9·90)

This volume consists of 10 chapters providing current information on drug therapy and ophthalmology. In glaucomato-cyclitic crises prostaglandins, particularly PGE, were found in high concentration in aqueous humour during the attack. Intraocular pressure and the aqueous PGE content could be correlated. Oil drops of indomethacin in concentrations of 0·5% were found to reduce postoperative inflammation following soft-cataract aspiration. It seems possible that miosis and postoperative inflammation are the result of prostaglandins.

Four cases were reported in which prolonged use of local anaesthetics resulted in the development of a yellowish white ring in the corneal stroma after primary epithelial disease, a corneal abrasion, or a contact lens injury.

The best intraocular irrigating solution—one which spares the endothelium—is glutathione bicarbonate

Ringer's solution followed by balanced salt solution. This information is particularly valuable in eye surgery on patients who already have corneal endothelial decompensation (corneal guttata) or on those who are undergoing phako-emulsification and pars plana vitrectomy.

There is a chapter on timolol, a beta-adrenergic blocking agent which shows great promise as a new drug for the treatment of glaucoma. It seems possible that the mechanism of action is by decreasing the secretion of aqueous humour. The duration of action is at least 24 hours in a concentration of 0·5%.

A slow release of artificial tears offers a new approach to the control of keratitis sicca. It offers a functional approach to an otherwise difficult and common clinical problem by producing a tear film that is clinically thicker than normal and retains fluid within it. It is a pliable rod composed solely of a water-soluble cellulose polymer and is inserted below the tarsus of the lower lid. It slowly dissolves and appears to provide in some patients great benefit.

Increased use of ointments may prove the most effective way of applying some drugs to the anterior segment of the eye. In animals sustained therapeutic levels in the tears, aqueous humour, and cornea are superior, with antibiotics in ointment used 4 times a day in contrast to once daily subconjunctival injections. Topical disodium cromoglycate drops produced significant improvement in 18 patients with vernal keratoconjunctivitis or atopic keratoconjunctivitis in a double blind placebo-controlled clinical trial.

The final chapter describes molecular alteration of epinephrine to produce a prodrug, dipivalyl epinephrine, that is a more potent adrenergic compound and better tolerated than standard epinephrine preparations.

S. J. H. MILLER

Notes

Retinal diagnosis and therapy

A 5-day course on techniques of retinal diagnosis and therapy will be held at the Institute of Ophthalmology, Cayton Street, London EC1V 9AT, between 27 November and 1 December 1978; suitable for consultants and senior registrars or overseas equivalent. Course fee £70.

Workshop on microsurgery 1978

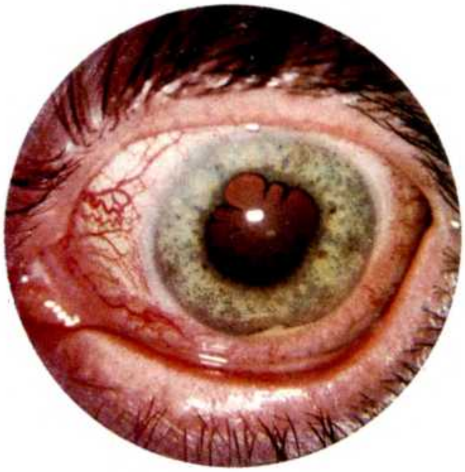
The Royal Australasian College of Surgeons will be organising a second teaching workshop on microsurgery in Singapore during 4–10 December 1978. The workshop is designed for surgeons who have never used the operating microscope or who are having adjustment difficulties. Further information from Dr Arthur S. M. Lim, Chairman, Workshop on Microsurgery, 441 Singapore Medical Centre, Tanglin Shopping Centre, 19 Tanglin Road, Singapore 10.

European Ophthalmic Pathology Society

The European Ophthalmic Pathology Society held its annual meeting in Belgrade, Yugoslavia, on 14–17 June 1978. Dr A. P. Ferry (Richmond, Virginia, USA) was the guest of honour. The scientific programme included 39 case presentations by members and guests, and 17 nations were represented. For each presentation a protocol, histopathological sections, and clinical or macroscopic transparencies were provided. Most of the case presentations dealt with benign or malignant neoplastic processes involving the globe, orbit, or eyelid, and the discussion was concerned predominantly with classification, prognosis, and management. Congenital malformations were also a prominent feature among the presentations, and the remainder of the cases provided examples of systemic disorders involving ocular or adnexal tissues. Thirty-one members attended and 7 guests.

Prevention of blindness

The first general assembly of the International Agency for Prevention of Blindness was held on 6–8 July at Oxford under the presidency of Sir John Wilson. The president said the primary purpose of the agency was to create a new climate of opinion in which immediate and decisive action could be taken to reduce the economic loss and human misery resulting from 40 million blind people in the world. Statistics from the United States International Eye Institute showed that unless decisive action was taken the number of blind people in developing countries might increase five-fold in less than 50 years. The assembly considered that adequate technology exists to reduce the 4 causes of eye disease which account for 80% of blindness in the developing world, namely, trachoma, xerophthalmia, onchocerciasis, and cataract. Another statistic showed that 250 000 people go blind annually from vitamin deficiency. According to the Director-General of the WHO, the prevention of blindness now represents one of the most advantageous options in the whole range of public health policy. The British Government has decided to make available to the Royal Commonwealth Society for the Blind the funds to enable it to continue to provide in the United Kingdom an administrative base for the agency.



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Thom Zimmerman, MD
Beta-Adrenergic Blocking Agents

Wednesday, January 17: INTRAOCULAR LENS/CATARACT SURGERY SEMINAR. Chairman: **Richard C. Troutman, MD,** State University of New York, Brooklyn. Speakers: **Drs Robert Abel, Robert Azar, John Beale, Jr., Charles Bechert III, Randall Bellows, Claes Dohlman, Wayne Fung, William Harris, Jack Hartstein, Kenneth Hoffer, Richard Kratz, Marvin Kwitko, Norman S. Levy, Harold G. Scheie, Edward L. Shaw, John P. Shock, William Simcoe, Robert M. Sinskey.**

Thursday, January 18: CORNEA AND EXTERNAL DISEASES SEMINAR. Chairman: **Herbert E. Kaufman, MD,** Louisiana State University, New Orleans. Speakers: **Drs Claes Dohlman, Miles Friedlander, Edward Grom, Enrique Gutierrez, Randall J. Olson, S. M. Recupero, Giuseppe Scuderi.**

CONTACT LENS SEMINAR. Chairman: **Antonio Gasset, MD,** University of Florida, Gainesville. Speakers to be announced.

Friday, January 19: VITREOUS/CHOROID/RETINA SEMINAR. Chairman: **Harvey Lincoff, MD,** Cornell University, New York. Speakers to be announced.

Program to include afternoon tutorials in Intraocular Lens Surgery, Strabismus, Ultrasonography, the Lacrimal System, External Ocular Diseases, Metabolic Eye Diseases, Beta-Adrenergic Blocking Agents in Glaucoma, Gonioscopy, Tonometry, and others.

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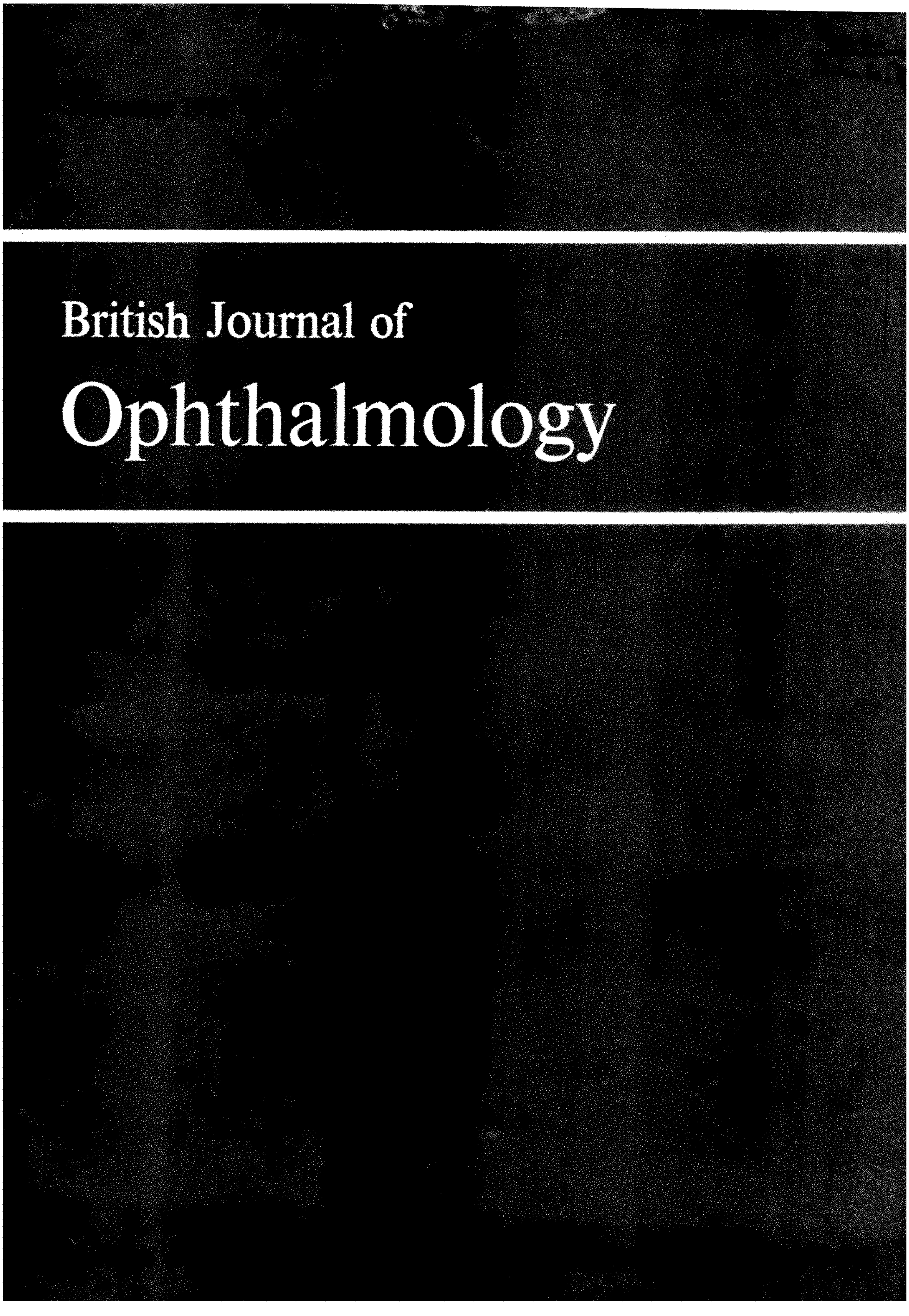

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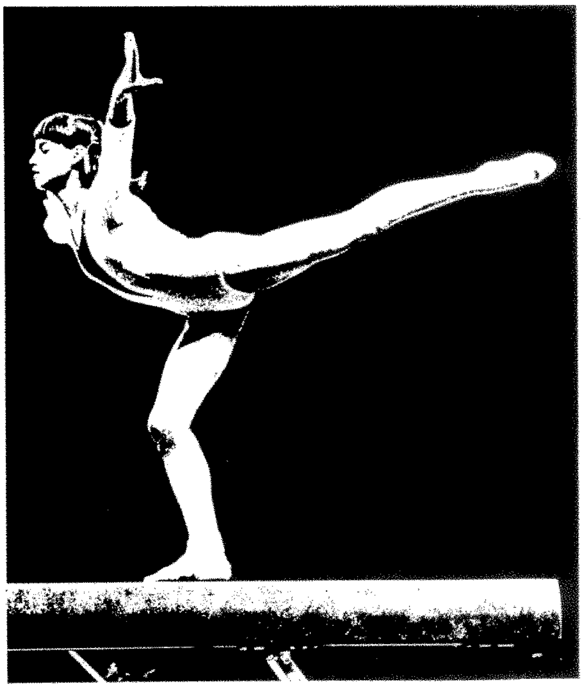

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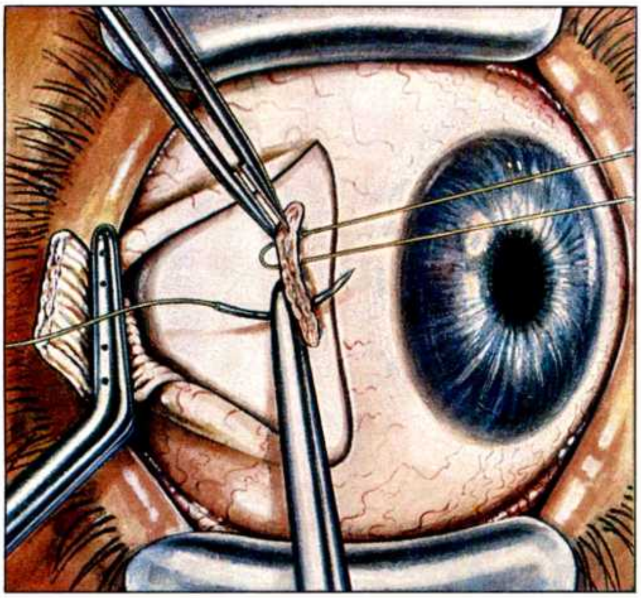

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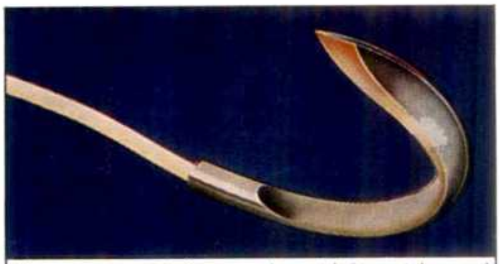

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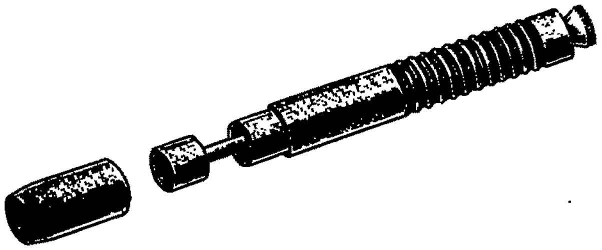

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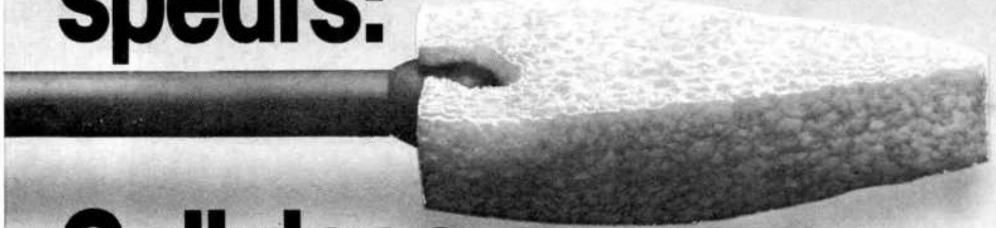

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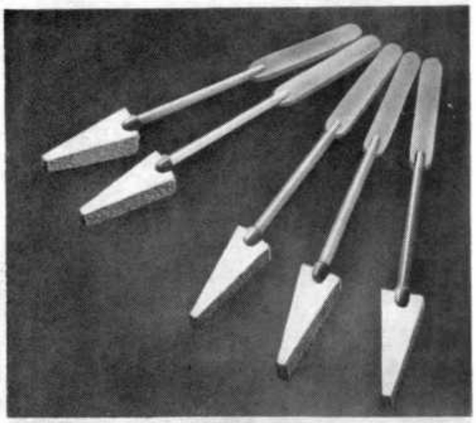

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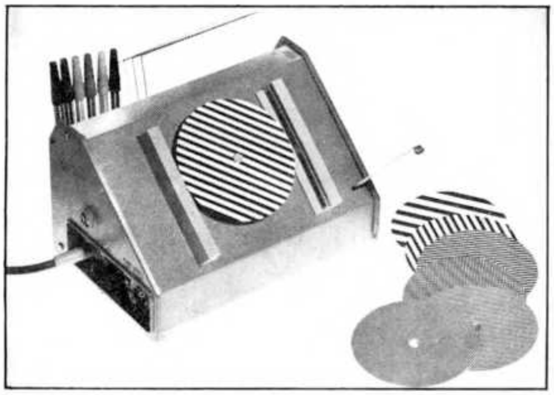

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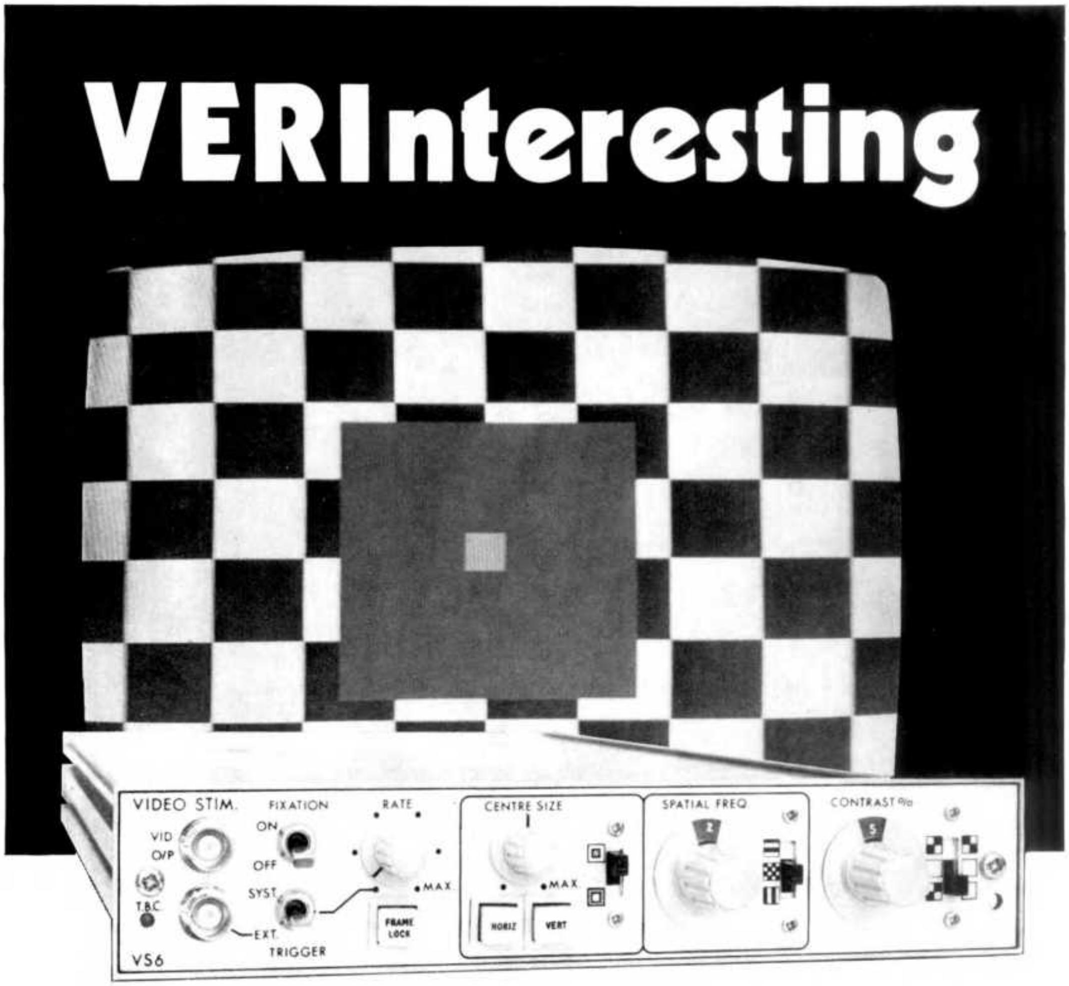

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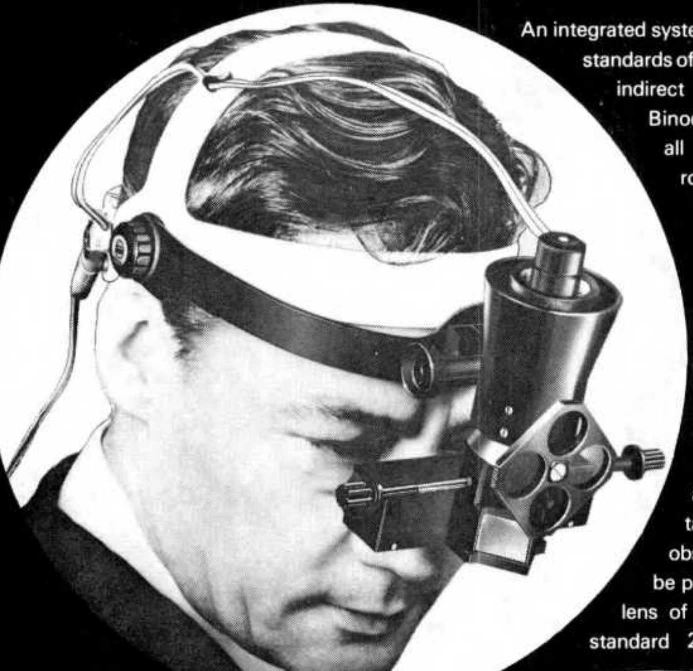

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Pathogenesis and classification of massive periretinal proliferation

ROBERT MACHEMER

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SUMMARY Massive periretinal proliferation (MPP), a serious complication of retinal detachment, is caused by proliferation and fibrous metaplasia of cells mostly deriving from retinal pigment epithelium and retinal glial cells. Contracting fibrous membranes in the vitreous, and on and also under the retina, cause the intraocular changes of MPP. Early signs such as increased 'tobacco dust', pigmented and unpigmented clumps in the vitreous, and subtle preretinal and even retroretinal membranes are usually overlooked. The late signs such as starfolds, irregular retinal folds, circumferential folds, and funnel-shaped detachments are well known. The pathogenesis of the clinically visible signs is described, and a 4-stage classification of the disease is given.

One of the most serious complications of retinal detachment is the development of excessive vitreous strand formation and fixed retinal folding. In accordance with its pathogenetic interpretation, this entity has been called massive vitreous retraction (MVR), massive preretinal retraction (MPR) (Tolentino *et al.*, 1967), massive preretinal fibroplasia (Cibis, 1965), or massive periretinal poliferation (MPP) (Machemer and Laqua, 1975). This complication accounts for the majority of failures in retinal surgery.

Evaluation of animal experiments (Machemer and Laqua, 1975; Mandelcorn *et al.*, 1975; Mueller-Jensen *et al.*, 1975; Laqua and Machemer, 1975a; Laqua and Machemer, 1975b) in which the human disease could be simulated, the analysis of the intraocular situation during vitreous surgery, and the study of specimens taken from the human eye have all helped us to understand the human disease better.

In this paper the author's experiences are combined to explain the pathogenesis of the disease in the human eye and to present a clinically useful classification of its various stages.

Pathogenesis of MPP

Experimental production of retinal detachment in owl monkey eyes (Machemer and Norton, 1968) has provided a unique opportunity to study in detail the development of massive periretinal proliferation (MPP). The clinical picture of MPP in this model is very similar in appearance to that in the human disease. Histological examination of human eyes with MPP and electron microscopic studies of specimens obtained from human eyes during vitrectomy also suggest the similarity of the animal model to the human disease (van Horn *et al.*, 1977).

Here an attempt is made to use the detailed knowledge gained from animal experiments and human studies to provide an explanation of the pathogenesis of MPP which is also valid for the human eye. Conclusions are based on the observations that cells undergoing proliferation and metaplasia probably deriving from retinal pigment epithelium (Machemer and Laqua, 1975; Mandelcorn *et al.*, 1975; Mueller-Jensen *et al.*, 1975; Machemer *et al.*, 1978) and from retinal glial cells (Laqua and Machemer, 1975a; van Horn *et al.*, 1977) are mostly responsible for this complication. The evidence for these two sources will be discussed in this order.

PIGMENT EPITHELIAL PROLIFERATION

When the retina is detached, cells are probably liberated from the pigment epithelium and appear as pigmented macrophages under the retina (Machemer and Laqua, 1975). Like normal pigmented epithelial cells in contact with the outer surface of the retina these cells continue to phagocytose outer segment material (Fig. 1). They multiply

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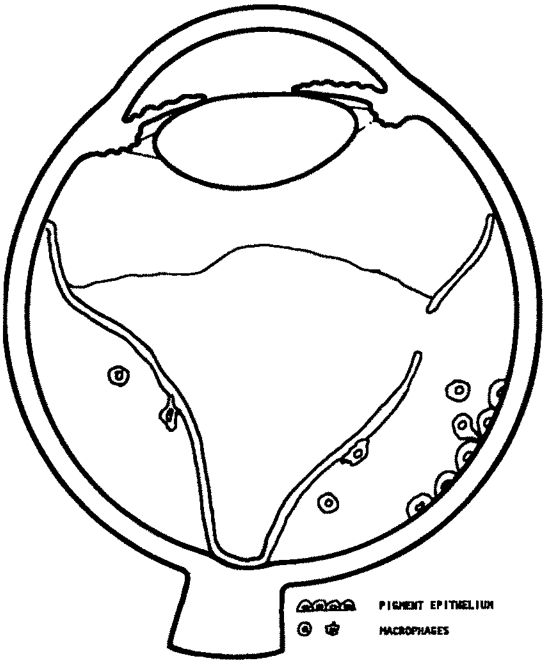

Fig. 1 *Schematic drawing of rhegmatogenous retinal detachment. Pigment epithelial cells from the pigment epithelial layer are liberated and become macrophages either freely floating in subretinal fluid or phagocytosing outer segment material*

and appear in the subretinal space as well as in the vitreous cavity (Fig. 2). Since the cells are not seen to migrate through the retina, they must reach the vitreous cavity through a retinal hole (Machemer and Laqua, 1975). The cells are usually visible as 'tobacco dust' (Hamilton and Taylor, 1972) in the vitreous and accumulate inferiorly on the surface of the retina.

Simultaneously some of the pigment epithelial macrophages undergo changes. A first group of cells begins to resemble fibroblasts and fibrocytes (Machemer and Laqua, 1975; Machemer *et al.*, 1978). As the fibroblast-like cells multiply, clusters and tissue membranes of these cells are found on any available surface—the inner retinal surface, vitreal surface, posterior lens surface, and even in the subretinal space along the outer surface of the retina (Machemer and Laqua, 1975; Laqua and Machemer, 1975b) (Fig. 3).

A second group of cells also develop cellular membranes. Except for their ectopic location they bear close similarity to normal pigment epithelium and are therefore called pigment epithelium cells (Machemer and Laqua, 1975). Both types of cellular membranes are initially clinically invisible and can only be suspected by their slight pigmentation. Since the cells all originate from cells that have undergone many cell divisions, and pigment is not renewed during this process, their pigment content is very low (Machemer and Laqua, 1975) (Fig. 3).

GLIAL CELL PROLIFERATION

In addition to the pigment epithelial cells retinal glial cells participate in the proliferative process during retinal detachment (Laqua and Machemer, 1975a; van Horn *et al.*, 1977). These cells grow through the internal limiting membrane and proliferate along the inner retinal surface, usually forming more localised membranes. Glial cells also protrude through the external limiting membrane of the retina and grow along its outer surface, sometimes covering large areas (Laqua and Machemer, 1975a) (Fig. 4).

CONTRACTION OF MEMBRANES

One of the most disastrous effects of massive periretinal proliferation is the sudden occurrence of contraction. A mechanism very similar to fibroblastic proliferation and contraction in wound repair (Peacock and Van Winkle, 1970) probably takes place inside the eye. Changed pigment epithelial

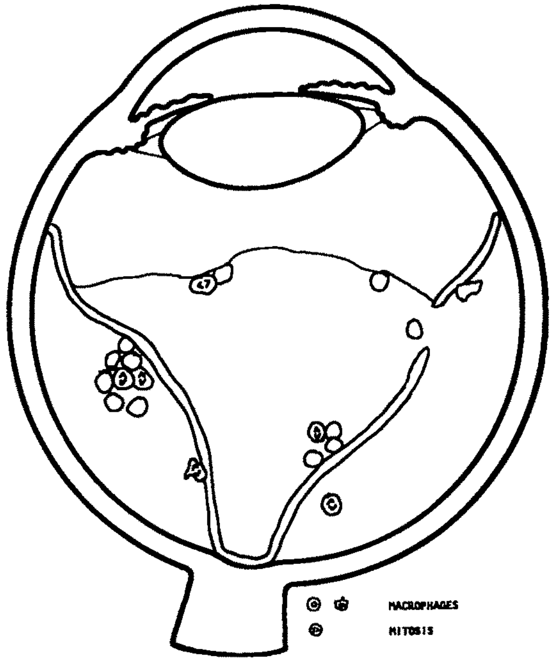

Fig. 2 *Macrophages have migrated through the retinal hole into the vitreous cavity and settled on the retinal surface or posterior vitreous membrane. Their number increases through cell division*

cells behave like fibroblasts; they multiply and migrate in the direction of cell-free space along available surfaces. They adhere to the underlying surfaces and to each other. As the cells move forward they are stretched, and tensile or contractile forces develop (Constable *et al.*, 1974).

Rather massive amounts of cytoplasmic filaments are found in the metaplastic pigment epithelium as well as in the proliferating glial cells (Machemer and Laqua, 1975; Laqua and Machemer, 1975a; van Horn *et al.*, 1977; Machemer *et al.*, 1978). Cytoplasmic filaments are a normal constituent of many cells. The exact importance of these filaments is not known, but it has been suggested that they may be contractile (Spoones *et al.*, 1971; Crawford *et al.*, 1972). The high content of these filaments in some of the membrane-forming cells makes it possible to speculate that it is this structure that causes contraction of the cells. Although cells are often not even interconnected by cell junctions, they seem to adhere to each other and form a membrane. It is this whole membrane that contracts.

Contractile forces are exerted very early in the development of the membranes. They are initially so minimal that changes remain invisible. The contractile forces finally become so strong that they are stronger than the structural or adhesive forces of the retina. Depending on the force and the size of the contracting membrane, different clinical pictures result that vary from superficial surface wrinkling to heavy folding of the retina (Figs. 5, 6). Along the vitreous scaffolds contraction can occur without being seen, since vitreous structure itself is normally barely visible. If these membranes are on the surface of the retina, they can exert an extensive pull on the retina, resulting in its folding and detachment. Sometimes these membranes may be so large and the forces build up to such a degree that their contraction detaches the entire retina.

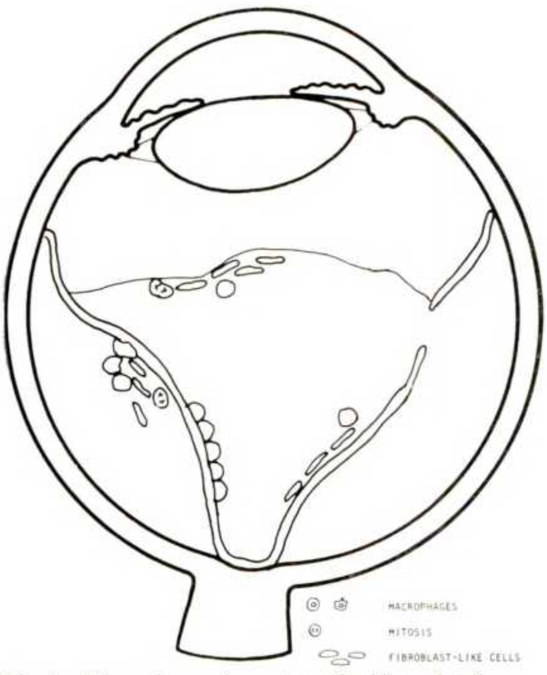

Fig. 3 *Macrophages change into fibroblasts that form membranes under the retina, on the retinal surfaces, and along the detached posterior vitreous. Multiplication continues*

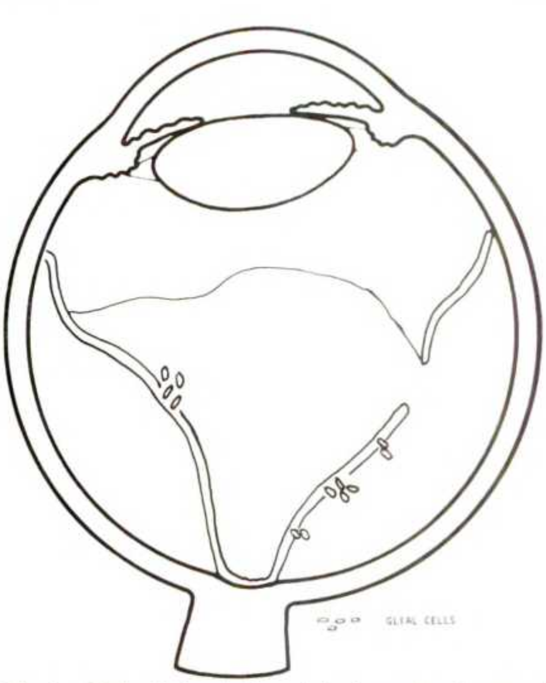

Fig. 4 *Glial cells break through the internal and external limiting membrane of the retina and begin to form membranes on and under the retina*

Experiments have shown that altered pigment epithelium can produce collagen (Machemer and Laqua, 1975; Mueller-Jensen *et al.*, 1975; Newsome and Kenyon, 1973). Many workers have thought in the past, and most recently (Havener, 1973; Algvere and Kock, 1976) that this collagen formation is the key to the contraction of these membranes. However, it is known that collagen does not contract and exhibits shortening only when denatured (Peacock and Van Winkle, 1970). Therefore it must be concluded that the cells themselves produce the contractile forces. Collagen does not participate in the contraction but only in the stabilisation of the contracture (Peacock and Van Winkle, 1970). It is

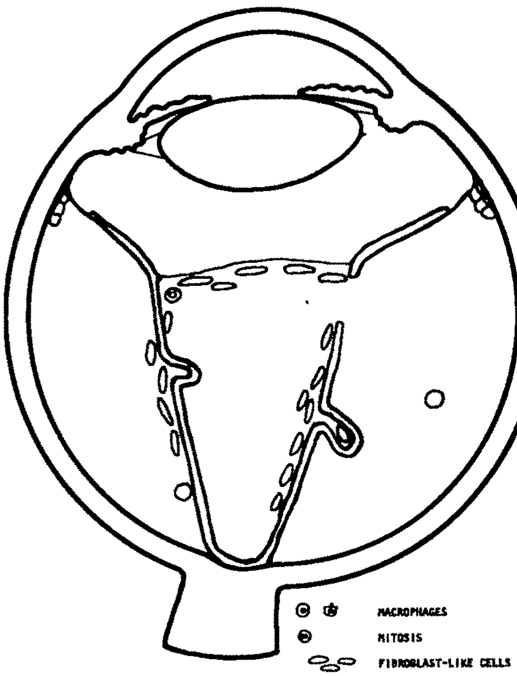

Fig. 5 *Pre- and subretinal fibroblastic membranes contract and throw the retina into folds. Posterior vitreous membrane is shortened, pulling the retina centrally. A funnel-shaped detachment results*

mainly the collagen component that makes the intravitreal tissue look whitish and forms the relatively solid intravitreal membranes (Fig. 7). Membranes are therefore not (or only to a very minor degree) condensations of pre-existing vitreous collagen. Preretinal membranes, which are practically invisible so long as they consist of only a simple cellular layer, lose their transparency after collagen deposition.

Definition of MPP

Massive periretinal proliferation (MPP) may thus be described as a condition of the eye with retinal detachment in which proliferation of cells along available surfaces—usually the vitreous, inner retinal, and outer retinal surfaces—results in membrane formation. The cells derive from pigment epithelium and retinal glia that have undergone metaplasia. The cellular membranes contract, causing the retina to fold and the vitreous framework to collapse. Deposition of collagen in the membranes renders them visible as semi-transparent intravitreal and preretinal strands and membranes.

Various pathogenetic mechanisms have been proposed in recent years to explain the development

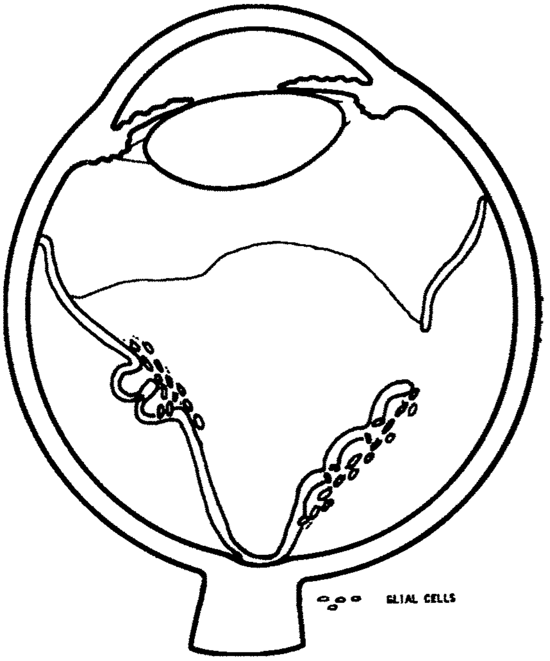

Fig. 6 *Contracting pre- and subretinal glial membranes can cause retinal folding*

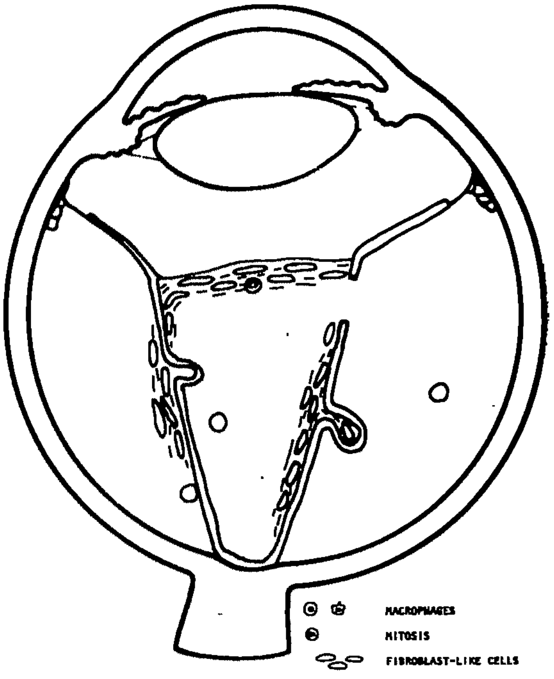

Fig. 7 *Collagen deposition between fibrocytes stabilises contracted cellular membranes*

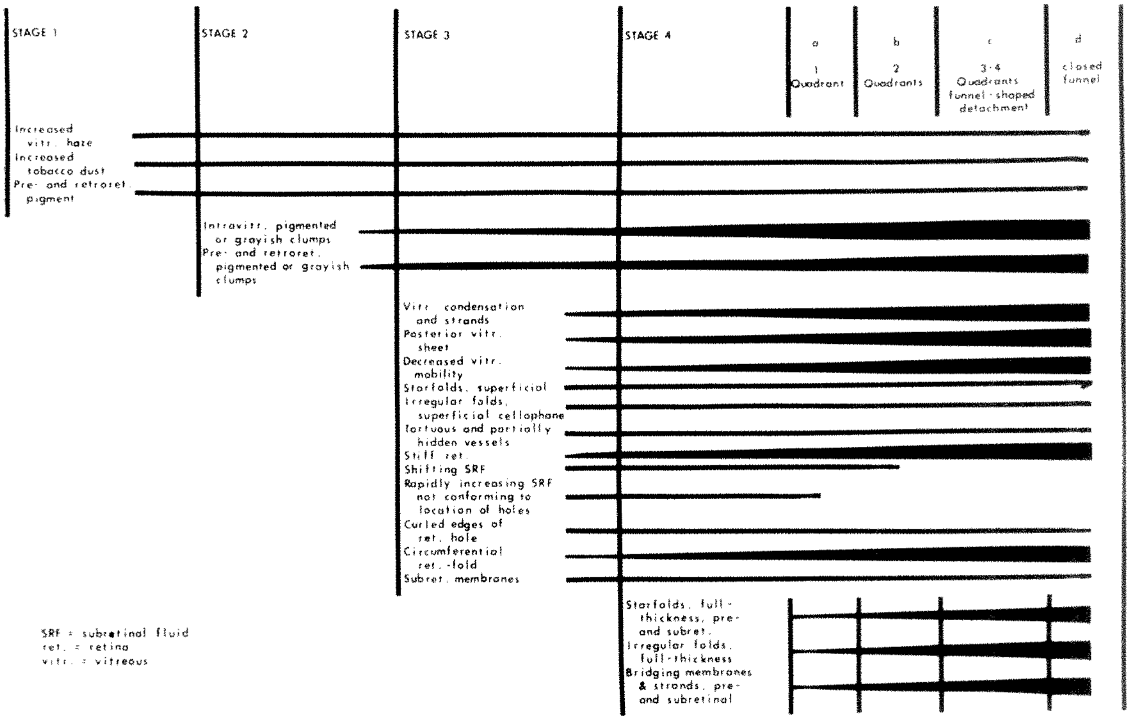
STAGE 1
STAGE 2
STAGE 3
STAGE 4
a
1 Quadrant
b
2 Quadrants
c
3-4 Quadrants funnel-shaped detachment
d
closed funnel
Increased vitr. haze
Increased tobacco dust
Pre- and retroret. pigment
Intravitr. pigmented or grayish clumps
Pre- and retroret. pigmented or grayish clumps
Vitr. condensation and strands
Posterior vitr. sheet
Decreased vitr. mobility
Starfolds, superficial
Irregular folds, superficial cellophane
Tortuous and partially hidden vessels
Stiff ret.
Shifting SRF
Rapidly increasing SRF not conforming to location of holes
Curled edges of ret. hole
Circumferential ret.-fold
Subret. membranes
Starfolds, full-thickness, pre- and subret.
Irregular folds, full-thickness
Bridging membranes & strands, pre- and subretinal
SRF = subretinal fluid
ret. = retina
vitr. = vitreous

Fig. 8 *Classification of massive periretinal proliferation (MPP). Continuous lines show presence of a symptom at the various stages. Expanding lines show increasing severity of a given symptom as the disease progresses*

and clinical picture of massive periretinal proliferation. Just as the name implies, shrinkage of vitreous alone was originally thought to be the cause of massive vitreous retraction (MVR).

Havener (1973) in a rather recent detailed article describing MVR still adheres to this theory. Interestingly, he speculates that anterior vitreous separates from the vitreous base, which retracts posteriorly and forms a frontal plane. This idea is used to explain why the anterior retina usually looks smooth whereas the posterior retina is crinkled and why a plane crossing the vitreous cavity is seen. If biomicroscopy has not already shown that vitreous is condensed in the anterior vitreous cavity, vitrectomy certainly has proved that the vitreous in MVR is tightly adherent to the vitreous base and is detached posteriorly.

Tolentino *et al.* (1976) states that massive preretinal retraction (MPR) is caused by cells growing along the retinal surface, the posterior vitreous surface, and in the vitreous. They consider that shrinkage of the vitreous and of membranes (perhaps triggered by heat of diathermy and photocoagulation or cold from cryoapplications) causes the picture of MPR. The fibroblastic appearance of the membranes and their collagen content is emphasised (Smith, 1960; Constable *et al.*, 1974). However, epithelial cells were seen as well.

Gloor (1976) agrees that MPR is caused by a proliferative process, but he thinks that it is caused by glial proliferation as suggested by the studies of Roth and Foos (1971), Foos (1974), Foos and Gloor (1975), and Rentsch (1973). He believes that tissue in the vitreous or along the posterior vitreous surface is actually a membrane that was 'ripped away' from the retina during vitreous detachment. Obviously, new proliferations of the retinal surface must occur to explain the folded retina behind such a posterior vitreous detachment. He also sees a continuum between macular fibrosis and massive preretinal retraction. I can agree with this observation only so long as spontaneous puckers are excluded. These are always localised and never end up in a massive shrinking process. In contrast, postoperative puckers after photocoagulation and buckling therapy of retinal holes can develop into a process involving the whole fundus. The localised nature of spontaneous puckers and the tendency of postoperative puckers occasionally to cause the full picture of MPP lets me assume that the latter are not solely caused by glial cells but rather by another type of cells, presumably cells deriving from the pigment epithelium.

Classification of MPP

One of the main difficulties in the interpretation or comparison of results in the surgical treatment of MPP is the lack of a classification to define the various stages of its severity. Present classifications have rather broad stages and neglect the early signs. Tolentino *et al.* (1967), for example, differentiate between 'early' and 'established'; Havener (1973) between 'possible', 'probable', 'definite', and 'advanced'; Scott (1975) between 'prefibrotic' and 'fibrotic'. For this reason I consider it is important to redefine MPP stages more precisely and show these as detailed as possible in Fig. 8. In reading the descriptions of the various stages, it will again become obvious how the full picture of MPP develops.

STAGE 1

The vitreous, normally transparent, begins to have a diffuse haze. Isolated pigment epithelial macrophages appear as fine brown dots under the retina in the vitreous cavity and tend to accumulate on the surface of the inferior retina. Under the retina they usually remain undetectable unless a convoluted retinal flap allows observation of the undersurface of the retina (Laqua and Machemer, 1975b). In the vitreous cavity the pigmented macrophages are known as 'tobacco dust' (Hamilton and Taylor, 1972). These findings are not typical simply for MPP but are encountered in practically all rhegmatogenous retinal detachments. However, the vitreous haze and the number of brown dots markedly increase in MPP.

STAGE 2

Further proliferation of the macrophages results in cluster formation. These clusters become visible clinically as lightly pigmented or greyish clumps in the vitreous cavity and on the retinal surface and also as yellowish brownish clumps under the detached retina (Machemer and Laqua, 1975; Machemer and Norton, 1968). The intravitreal clumps have been described by Havener (1973), Scott (1976), and Tolentino *et al.* (1967). Whereas 'tobacco dust' (Hamilton and Taylor, 1972) represents only a large number of isolated macrophages (Machemer and Laqua, 1975), clump formation is the first indication of cells beginning to stick together and to form membranes (Machemer and Laqua, 1975; Laqua and Machemer, 1975b).

STAGE 3

Often the third stage of MPP is not fully appreciated clinically although it contains all the features that to a larger extent occur in full-blown MPP. The critical point is that cellular membranes are now developed along all the available surfaces.

The vitreous at this stage begins to show increased density and to develop a membrane along its detached posterior surface (Tolentino *et al.*, 1967; Havener, 1973). Strands seen in the anterior vitreous may fuse with this membrane. Often the membrane has one or more round to oval openings or gaps, which often contain vitreous with an anteroposterior orientation of fibrils (Havener, 1973). The membranes are under tension and decrease the mobility of the vitreous.

Preretinal membranes are often not visible as such, though secondary changes are indicative of the membrane.

I have been able to verify in man the tiny superficial starfold which was seen in animal experiments (Laqua and Machemer, 1975b), which wrinkles only the surface of the retina in a very localised area (Fig. 9). This is possible only when the vitreous is clear enough to allow good visualisation of the retina and with the help of a contact lens and high magnification.

Large thin membranes on the surface of the retina cause irregular reflexes (cellophane appearance) because of wrinkling of the internal limiting membrane and irregularities on the membrane surface. Vessels become less visible. Slight contraction of the membranes results in tortuosity of the vessels (Laqua and Machemer, 1975b) (Fig. 10) or in their stretching outside the area of the membrane. The retina becomes stiff. Normal detached retina undulates easily after quick eye movements; the retina in MPP retains its position nearly unchanged. Together with this one observes a shifting of the subretinal fluid, which is an indication that the retina, though seemingly flattened, is no longer adherent to the pigment epithelium. The increasing preretinal membrane formation and the consequent

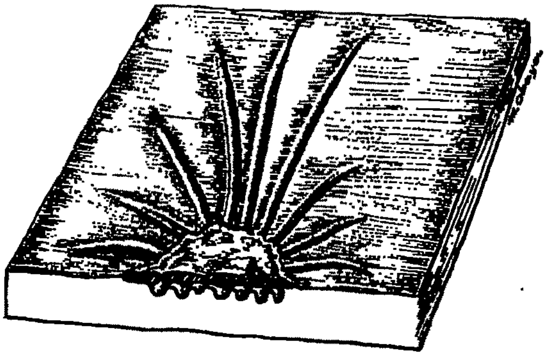

Fig. 9 *Tiny superficial starfold created by small preretinal membrane folding superficial layers only* (*Permission* American Journal of Ophthalmology)

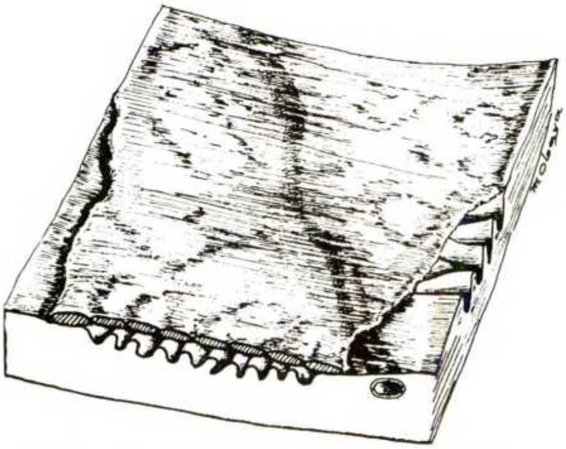

Fig. 10 *Schematic drawing of preretinal membrane causing tortuosity and obscuration of vessels and also crinkling of internal retinal layer* (*Permission* American Journal of Ophthalmology)

stiffening of the retina also account for the fact that the location of the subretinal fluid no longer conforms to the location of the retinal hole.

Impressive changes also occur at the edges of the retinal holes. Since there is relatively little resistance to contraction of these small preretinal membranes, the posterior edges of the holes tend to curl inwards. This sign has recently been emphasised by Scott (1976).

It is difficult to demonstrate thin subretinal membranous sheets when seen through an altered retina. However, they do exist and have in fact been peeled from the undersurface of a folded retina during vitreous surgery by the author.

STAGE 4

During the fourth stage membranes become more pronounced. They are contracted heavily and are visible because of increased collagen deposits.

The posterior vitreous membrane is very prominent and the anterior vitreous is heavily condensed and contains strands and pigmented cell clusters. With further contraction of the posterior vitreous membrane and with the retina being pulled increasingly towards the centre of the eye the space in the anterior vitreous cavity is reduced. Vitreous may be forced posteriorly through the gaps in the posterior vitreous membrane. This explains the anteroposterior orientation of the vitreous fibrils seen in these holes.

Contraction of localised preretinal membranes typically leads to the formation of isolated, full-thickness starfolds (Laqua and Machemer, 1975b) with a depressed centre and converging folds that stop just before the centre (Figs. 11*a, b*). Contraction of a localised subretinal membrane also causes a full-thickness starfold very similar in appearance to the better-known preretinal one (Laqua and Machemer, 1975b). Careful analysis of this fold reveals that the centre is raised instead of depressed and that the radiating folds are centripetally connected to each other instead of terminating before the centre (Figs. 12*a, b*).

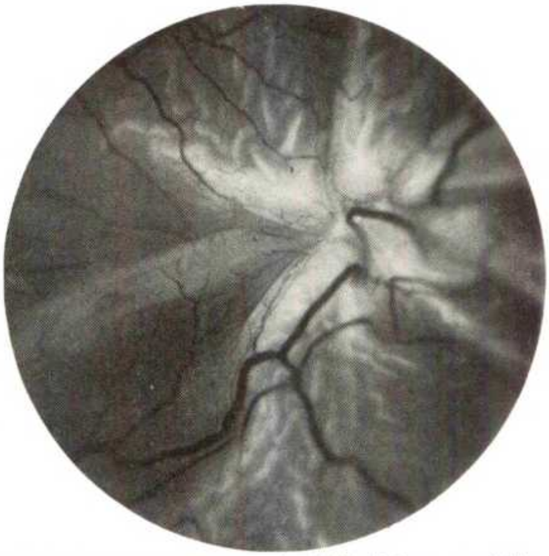

Fig. 11a *Clinical photograph of full-thickness starfold caused by preretinal proliferation. Note the depressed centre and the converging folds stopping just before the centre*

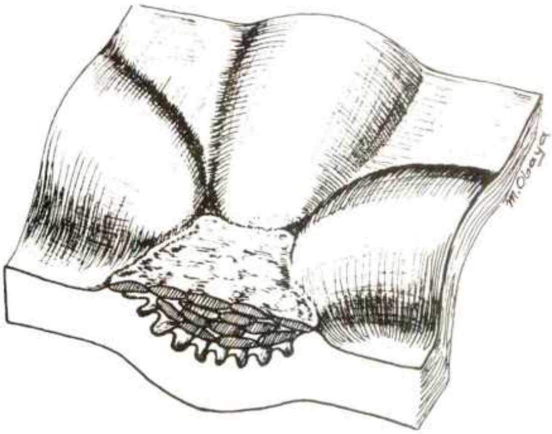

Fig. 11b *Schematic drawing of full-thickness starfold caused by preretinal proliferation* (*Permission* American Journal of Ophthalmology)

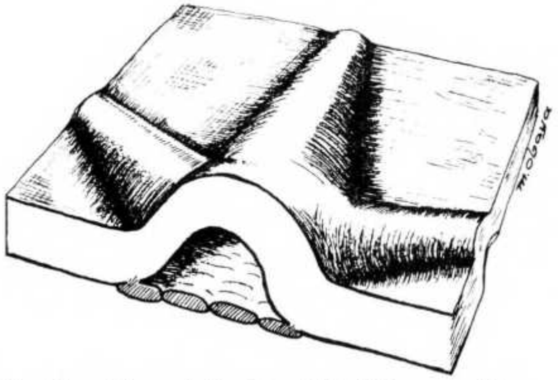

Fig. 12a *Schematic drawing of full-thickness starfold caused by retroretinal proliferation. Note the raised centre and the folds that are in connection with each other* (*Permission* American Journal of Ophthalmology)

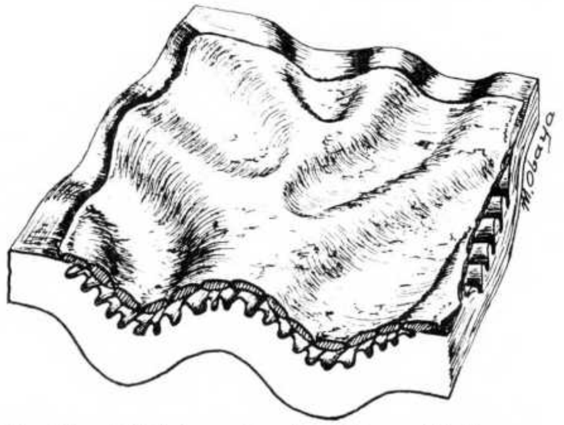

Fig. 13a *Full-thickness irregular fold caused by large contracting preretinal membrane* (*Permission* American Journal of Ophthalmology)

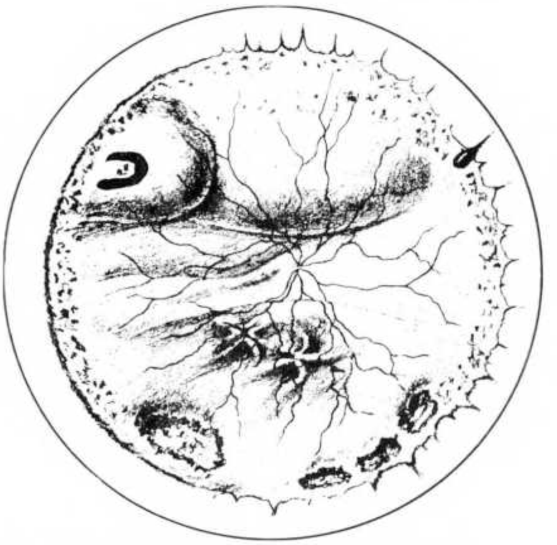

Fig. 12b *Drawing of full-thickness starfolds with preretinal* (left) *and retroretinal proliferation* (right) *(taken with permission from Schepens (1960))*

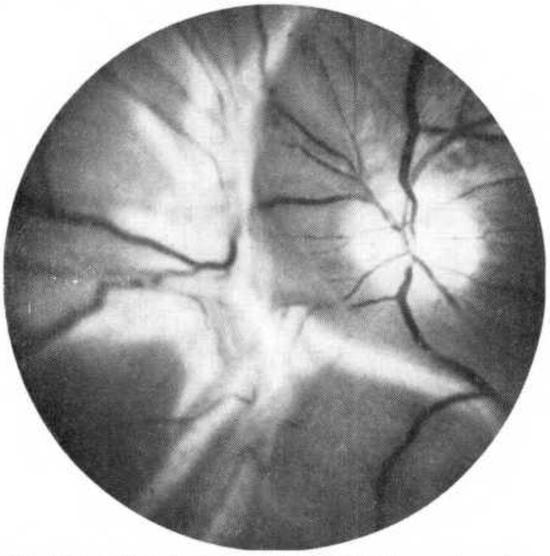

Fig. 13b *Clinical photograph of full-thickness irregular fold. Tightly packed folds in which vessels disappear and bridging preretinal strands are visible*

The retina is now irregularly folded; it looks thickened and has a yellow colour. These folds can be caused by a shrinking preretinal membrane (Fig. 13*a*) and are called full-thickness irregular folds. One is sometimes able to recognise strands bridging across the cascade-like retinal folds, but usually the folds are simply pulled tightly together. Vessels disappear completely in these folds (Fig. 13*b*). Subretinal folds—difficult to diagnose clinically but confirmed at vitreous surgery in folded-over retina—can also cause the full-thickness of the retina to fold (Fig. 14).

Very typical for this stage is the development of a circumferential retinal fold, which is usually located in the equatorial plane. First suggestions of this fold begin to show in stage 3. The fold represents the border between the detached posterior vitreous surface and the adherent vitreous base, and often presents itself as an irregular, peripheral, greyish ring-like structure (Fig. 15). It is interesting to note that, while the retina posterior to the circumferential fold is usually irregularly folded, it is flat anteriorly except for some radial folds. This phenomenon can be understood when one remembers that cells

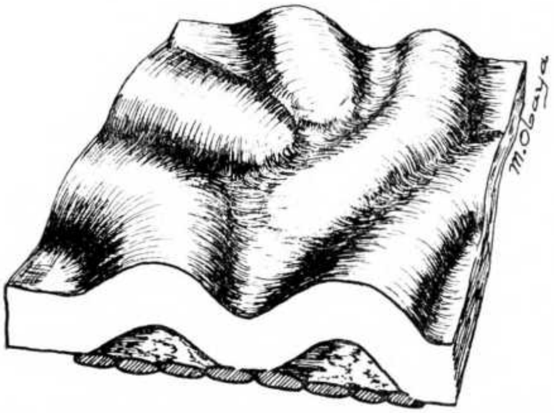

Fig. 14 *Full-thickness irregular fold caused by subretinal membrane contraction (permission* American Journal of Ophthalmology)

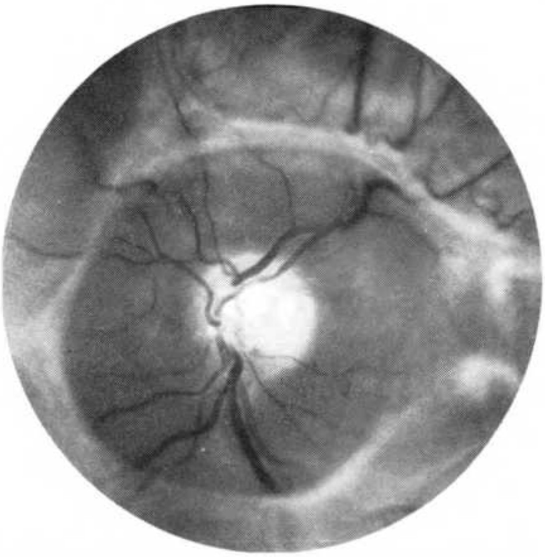

Fig. 15 *Clinical photograph of circumferential retinal fold caused by a greyish ring of fibrous tissue. In this specific case the fold is well visible, since retina is not folded posteriorly*

proliferate only along available surfaces. The vitreous base is still covered by vitreous and the proliferating cells do not have access to the peripheral retinal surface. In addition the contracting posterior vitreous membrane exerts a pull on the peripheral retina and stretches it (Fig. 16).

When all the posterior retinal surface is folded and the posterior vitreous plane has contracted, the typical funnel-shaped picture of MPP has developed, with the anterior retina in a frontal plane and the posterior retina forming a steep funnel (Fig. 17*a*). The contraction of the posterior vitreous surface can be so intense that eventually the disc itself may become invisible and the funnel entirely closed (Fig. 17*b*).

Because of the irregular surface of the retina and its decreased transparency it is very difficult to visualise anything that occurs underneath. But occasionally one will see definite strands after the retina has been reattached. These appear as straight, sometimes pigmented lines. These subretinal strands originally were part of a subretinal membrane.

This subretinal membrane does not adhere strongly to the retina (Laqua and Machemer, 1975a). When it begins to contract, it tears in those areas with the least thickness and the least tensile strength. Large holes develop in the membrane, and only the walls between the holes remain visible.

Finally, in the attempt to classify fully the changes of MPP for descriptive and therapeutic purposes I have found it necessary to subgroup this stage 4. The subgroupings represent an ever increasing amount of pathology. Group 4*a* represents a stage in which the lesion is confined to 1 quadrant; 4*b* has involvement of 2 quadrants; 4*c* involves 3 to 4 quadrants with a 'morning glory' appearance of the retina; in 4*d* the funnel of the detached retina is so narrow that the disc becomes invisible. Groups 4*a* and *b* have been treated surgically with conventional buckling procedures and successes have been

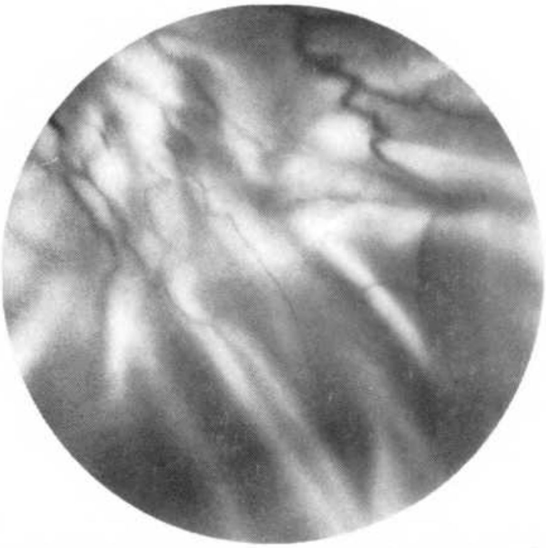

Fig. 16 *Clinical photograph of peripheral retina in MPP. While the posterior retina is heavily folded, the peripheral retina appears stretched with some radial folds only. In this case the fibrous ring is not visible*

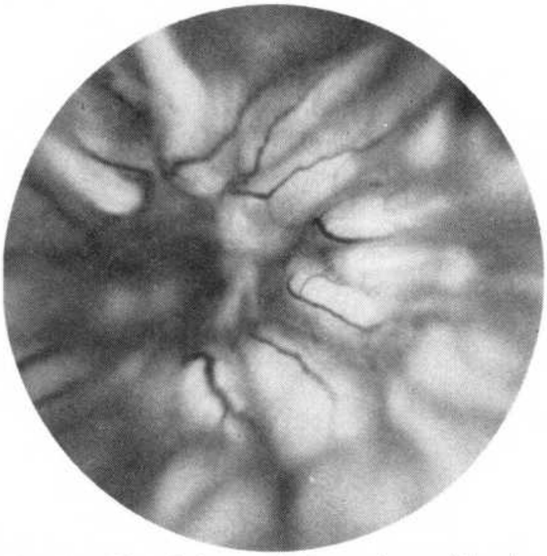

Fig. 17a *Clinical photograph of central part of funnel-shaped detachment with grade 4c MPP. Multiple cascade-like tightly packed full-thickness retinal folds in 3 quadrants pull the retina centrally. Note that the disc is still visible (out of focus)*

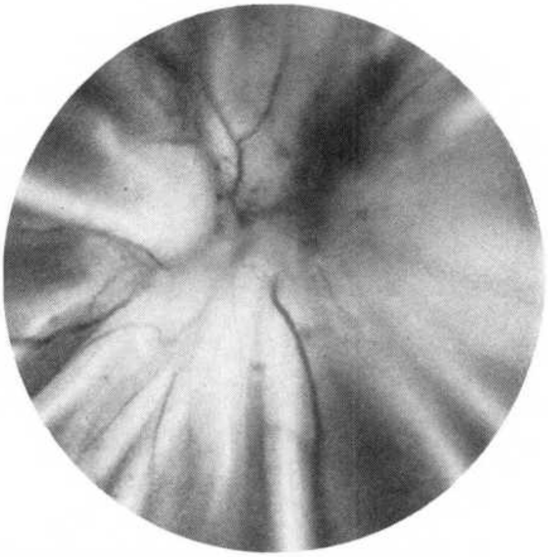

Fig. 17b *Clinical photograph of retina with closed funnel (grade 4d MPP). Pigmented tissue pulls retina together so tightly that the disc is invisible. Peripheral retina is stretched and has only radial folds*

achieved. Group 4*c* constitutes the present domain for intravitreal silicone injections. No successes have been reported in Group 4*d*. A justification for vitreous surgery with removal of the vitreous and preretinal membrane peeling increases from Group 4*a* to 4*d*.

Conclusion

MPP presents a tremendously wide range varying from proliferation of a few macrophages under a detached retina or on the retina and in the vitreous cavity to localised or, finally, generalised membrane formation and contraction of pigment epithelial and glial cells. This proliferation may become stationary or it may continue over many months at a low level, or it may be explosive, creating within hours the full-blown picture of MPP.

For the clinician it is of vital importance to find the earliest possible signs so as to have some idea of the impending disaster. I think that pigmented or greyish cell clusters in the vitreous cavity are probably the most important early clinical signs of active proliferation of cells. Together with increased vitreous haze they represent the first warning signs of possible impending complications. However, one must keep in mind that the proliferative process can stop at any stage during the development of MPP and that it still remains impossible to predict in a given case that a specific lesion will develop further.

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References

Algvere, P., and Kock, E. (1976). Experimental fibroplasia in the rabbit vitreous. Retinal detachment induced by autologous fibroblasts. *Albrecht von Graefes Archiv für klinische und experimentelle Ophthalomolgie*, **199**, 215–222.

Cibis, P. (1965). *Vitreoretinal Pathology and Surgery in Retinal Detachment*. Mosby: St. Louis.

Constable, I. J., Tolentino, F. I., Donovan, R. H., and Schepens, C. L. (1974). Clinical-pathologic correlation of vitreous membranes. In *Retina Congress*, pp. 245–257. Edited by R. C. Pruett and Ch. D. J. Regan. Appleton-Century-Crofts: New York.

Crawford, B., Cloney, R. A., and Cahn, R. D. (1972). Cloned pigmented retinal cells. The effects of cytochalasin on ultrastructure and behaviour. *Zeitschrift für Zellforschung*, **130**, 135–152.

Foos, R. Y. (1974). Vitreoretinal juncture—simple epiretinal membranes. *Albrecht von Graefes Archiv für klinische und experimentelle Ophthalomolgie*, **189**, 231.

Foos, R. Y., and Gloor, B. P. (1975). Vitreoretinal juncture; healing of experimental wounds. *Albrecht von Graefes Archiv für klinische und experimentelle Ophthalomolgie*, **196**, 213.

Gloor, B. P. (1976). Macular fibrosis and massive preretinal retraction. *Documenta Ophthalmologica Proceedings Series, New Developments in Ophthalmology*, Vol. 7, p. 105. Edited by A. F. Deutman.

Hamilton, A. M., and Taylor, W. (1972). Significance of pigment granules in the vitreous. *British Journal of Ophthalmology*, **56**, 700–702.

Havener, W. H. (1973). Massive vitreous retraction. *Ophthalmic Surgery*, **4**, 22–67.

Laqua, H., and Machemer, R. (1975a). Glial cell proliferation in retinal detachment (Massive periretinal proliferation). *American Journal of Ophthalmology*, **80**, 602–618.

Laqua, H., and Machemer, R. (1975b). Clinical-pathological correlation in massive periretinal proliferation. *American Journal of Ophthalmology*, **80**, 913–929.

Machemer, R., and Laqua, H. (1975). Pigment epithelial proliferation in retinal detachment (Massive periretinal proliferation). *American Journal of Ophthalmology*, **80**, 1–23.

Machemer, R., and Norton, E. W. D. (1968). Experimental retinal detachment in the owl monkey. I. Methods of production and clinical picture. *American Journal of Ophthalmology*, **66**, 388–395.

Machemer, R., van Horn, D. L., and Aaberg, T. M. (1978). Pigment epithelial proliferation in human retinal detachment with massive periretinal proliferation. *American Journal of Ophthalmology*, **85**, 181–191.

Mandelcorn, M., Machemer, R., Fineberg, E., and Hersch, S. B. (1975). Proliferation and metaplasia of intravitreal retinal pigment epithelial cell autotransplants. *American Journal of Ophthalmology*, **80**, 227–237.

Mueller-Jensen, K., Machemer, R., and Azarnia, R. (1975). Autotransplantation of retinal pigment epithelium in intravitreal diffusion chambers. *American Journal of Ophthalmology*, **80**, 530–537.

Newsome, D. A., and Kenyon, K. R. (1973). Collagen production *in vitro* by the retinal pigmented epithelium of the chick embryo. *Developmental Biology*, **32**, 387–400.

Peacock, E. E., and Van Winkle, W. (1970). *Surgery and Biology of Wound Repair*, p. 49. Saunders: Philadelphia.

Rentsch, F. J. (1973). Preretinal proliferations of glial cells after mechanical injury of the rabbit retina. *Albrecht von Graefes Archiv für klinische und experimentelle Ophthalomolgie*, **188**, 79.

Roth, A. M., and Foos, R. Y. (1971). Surface wrinkling retinopathy in eyes enucleated at autopsy. *Transactions of the American Academy of Ophthalmology and Otolaryngology*, **75**, 1047.

Schepens, C. L. (1960). Importance of the Vitreous Body in Retina Surgery with Special Emphasis on Reoperation. Mosby: St. Louis.

Scott, J. D. (1975). The treatment of massive vitreous retraction by the separation of preretinal membranes using liquid silicone. *Modern Problems in Ophthalmology*, **15**, 285–290.

Scott, J. D. (1976). Treatment of massive vitreous retraction. *Transactions of the Ophthalmological Societies of the United Kingdom*, **95**, 429–432.

Smith, T. (1960). Pathologic findings after retina surgery. In *Importance of the Vitreous Body in Retina Surgery with Special Emphasis on Reoperations*, p. 61–93. Edited by C. L. Schepens. Mosby: St. Louis.

Spoones, B. S., Yamada, K. M., and Wessels, N. K. (1971). Microfilaments and cell locomotion. *Journal of Cell Biology*, **49**, 595–613.

Tolentino, F. I., Schepens, C. L., and Freeman, H. M. (1967). Massive preretinal retraction. *Archives of Ophthalmology*, **78**, 16–22.

Tolentino, F. I., Schepens, C. L., and Freeman, H. M. (1976). *Vitreoretinal Disorders, Diagnosis and Management*, p. 479–489. Saunders: Philadelphia.

van Horn, D. L., Aaberg, T. M., Machemer, R., and Fenzl, R. (1977). Glial cell proliferation in human retinal detachment with MPP (Massive periretinal proliferation). *American Journal of Ophthalmology*, **84**, 383–393.

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Preliminary results of a physiologically based treatment of amblyopia

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SUMMARY An apparatus has been developed in which high-contrast square-wave gratings are rotated in front of the amblyopic eye while the child is performing some task requiring visual concentration. In the course of three 7-minute treatments 73% of patients treated achieved 6/12 or better; 75% of these patients had previously undertaken conventional or minimal occlusion.

Over the past decade neurophysiological experiments have demonstrated that the animal visual system is highly tuned for spatial frequency and orientation (Campbell *et al.*, 1968; Campbell *et al.*, 1969; Maffei and Fiorentini, 1973; Robson, 1975). Independent psychophysical experiments on man (for review see Campbell, 1974) substantiate that both spatial frequency and orientation are 'des pudels Kern' (Granit, 1974; 1977) for human vision.

Interest in amblyopia has recently been revived among physiologists because an understanding of its neural basis may have an important bearing on development theories of sensory function. Although this recent approach (Campbell, 1974) has been usefully applied to the investigation of the neural abnormality in amblyopia (Gstalder and Green, 1971; Levi and Harwerth, 1977; Hess and Howell, 1977) it has not yet been applied to the treatment of amblyopia.

The main rationale of amblyopia therapy has remained, with a few minor exceptions, unchanged for over 200 years (de Buffon, 1746). Although more recently pleoptics has developed in an attempt to centralise fixation, occlusion therapy in one form or another (for review see Hess, 1971) is still the most widely used and successful technique. Conventional full-time occlusion of the normal eye in patients who have macular fixation improves visual acuity to 6/12 or better in 88% (Catford, 1967). This figure falls to between 40 and 60% in patients who have eccentric fixation (Dayson, 1968; Pope, 1971; Olivier and Nawratzki, 1971; Piligrim and Turner, 1974). Full-time conventional occlusion, although it does sometimes produce dramatic and rapid improvement (Chavasse, 1939), usually has to be continued for between 3 and 18 months to achieve this level of improvement. It is a tedious and educationally disruptive technique, and its failure rate is high.

As an alternative to total occlusion we have recommended occlusion of the good eye every day for only 20 minutes while intensive close work was being undertaken; this achieved much better cooperation from the mother. With this treatment 83% of children improved their acuity to 6/12 or better (45% to 6/9) in the amblyopic eye. It produced an improvement in acuity disproportionate to its short duration, but it did take an average of 13 weeks to achieve this.

The surprising finding of the relative efficacy of 'minimal occlusion' led one of us (FWC) to consider what would be the most effective stimulus for the visual system during this limited period. Recent neurophysiological findings in animals and man (Robson, 1976; Campbell, 1974) suggest that to activate fully the entire population of visual neurones in the visual cortex a range of different spatial frequency gratings covering all orientations should be used. These criteria are best met by using a repetitive grating pattern with sharp luminance edges slowly rotating through 180°. This stimulus, which is based on current neurophysiological findings, was constructed (Banks *et al.*, 1978) and is being tested on a wide selection of amblyopic children. The preliminary findings, which are reported here, suggest that this new approach improves vision in the amblyopic eye much faster and more completely than any other technique.

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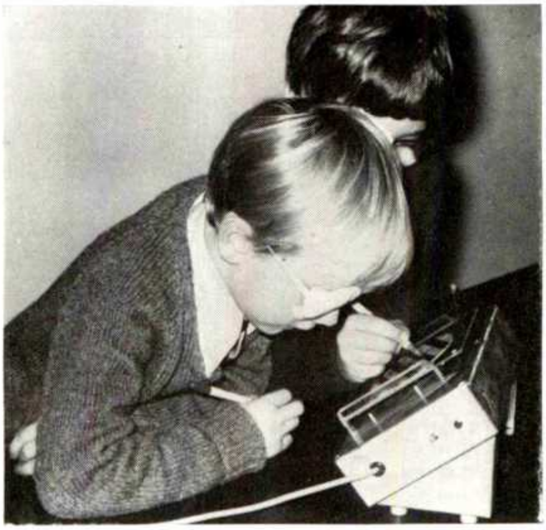

Fig. 1 *The grating treatment device in use*

The simplicity and low cost of the method has encouraged us to publish these early results so that the treatment can be assessed on a much greater number of children and adults.

Patients and methods

Treatment consists in viewing an apparatus on which any one of a selection of high-contrast square-wave gratings are rotated slowly at 1 revolution per minute behind a transparent cover on which drawing games can be played. Occlusion was used (only during the test) to limit vision to the amblyopic eye. If possible, 2 patients of equal age and intelligence were seated side by side in front of the apparatus with the non-amblyopic eye occluded (Fig. 1). The intended distance from the eye of the patient to the grating disc was 57 cm, but almost all the children worked closer than this. If only 1 patient was being treated, the orthoptist acted as the opponent in the game for the duration of the treatment.

The length of treatment was standardised so that the patient was observing the gratings for 7 minutes. The selected grating to be used was placed on the turntable; the Perspex plate was placed over this, and the patients were given drawing pens. The patients were then instructed, according to age and abilities, to play 'noughts and crosses', 'hangman', 'squares', or 'boxes', or to draw pictures, while the grating was rotating under the Perspex plate. This procedure forced the child to attend to the underlying stimulus.

All patients had a full ophthalmological examination, cycloplegic refraction, and orthoptic assessment, although it was not possible to fully assess binocular functions in all of them. The majority of children tested (75%) had previously undertaken partial or constant total occlusion, which had at best been only partially effective. Before any treatment was administered, visual acuity was assessed by the Snellen or linear Sheridan Gardiner optotypes and Sheridan single optotypes at 6 and 0·33 m. In those patients who had been recently accepted for treatment contrast thresholds for both a low and medium spatial frequency grating were assessed with simplified clinical plates.

These plates were circular and consisted of a sine grating each at a different contrast level near threshold. Each plate was presented to the child firstly at the highest contrast, and the child indicated its orientation. The contrast at which this task could not be performed was taken as the threshold. Normal and amblyopic eyes were tested with this technique for a low as well as a medium frequency grating.

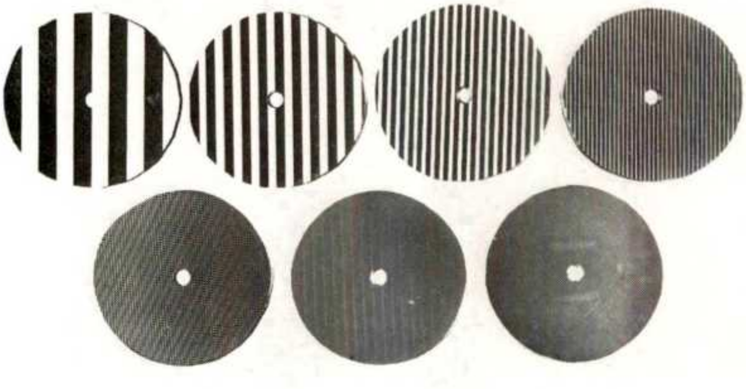

Fig. 2 *Range of grating stimuli used*

More recently the information derived from this simple and quick clinical test was used to select the initial spatial frequency used in the subsequent treatment and to assess (along with acuity measurements) its effectiveness. For example, if this test indicated that the amblyopic abnormality was limited to only medium to high frequencies (Gstalder and Green, 1971; Hess and Howell, 1977), then only spatial frequencies in this range were selected for treatment and subsequent assessment. On the other hand if the amblyopic abnormality extended to include low as well as high frequency gratings (Hess and Howell, 1977), a low spatial frequency grating was selected initially. Fixation of the amblyopic eye was assessed by projection ophthalmoscopy.

In the first group of patients all the gratings were used in sequence within a 7 minute treatment period, the treatment starting with a low frequency (0·5 c/deg) and working to the highest (32 c/deg). The abbreviated contrast threshold technique, which has already been discussed, was later adopted and found to be also satisfactory. If low frequencies were found to be abnormal, treatment was started at 0·5 c/deg, whereas if only medium to high frequencies were found to be abnormal treatment was started at 8 or 16 c/deg. In most patients at least 2 gratings were used during each 7-minute treatment period. In certain patients an unstructured disc (with no grating) was used as a control. After treatment linear Snellen and Sheridan Gardiner acuities and Sheridan Gardiner single optotypes were reassessed at 6 and 0·33 m, and contrast threshold was also reassessed. The visual acuity after treatment was always assessed, but if concentration was suspect it was not assessed before treatment began.

The patient was then sent home with specific instructions *not* to occlude the non-amblyopic eye. The majority of patients were treated at weekly intervals. A few were treated at home on a daily basis under the supervision of their parents if they were unable to attend regularly.

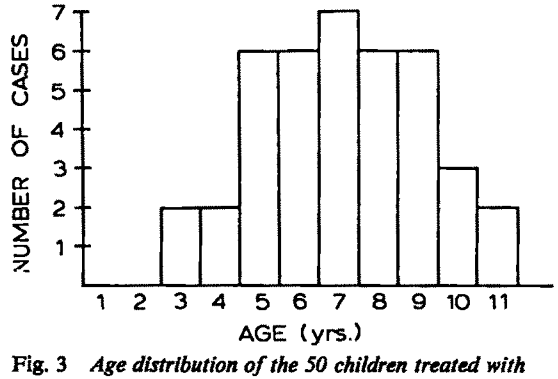

Fig. 3 *Age distribution of the 50 children treated with the grating stimulus*

Table 1

	Strabismic amblyopia			*Anisometropic amblyopia*		
	Nystagmoid fixation movements			*Nystagmoid fixation movements*		
	Yes	*No*	*Total*	*Yes*	*No*	*Total*
Without vertical imbalance	7	4	11	2	7	9
With vertical imbalance	19	9	28	—	1	1
Astigmatisms—both eyes	8	5	13	—	3	3
Amblyopic eye	7	5	12	1	2	3
Eccentric fixation	13	6	19	—	—	—
Anisometropia	16	10	26	2	8	10

Two patients attended the clinic daily for treatment. The treatment was continued until there was no further improvement in visual acuity or until the visual acuity was equalised in both eyes. After this the visual acuity and binocular functions were reassessed at 2- or 4-weekly intervals to ensure that no deterioration occurred.

Results

Of the 50 patients treated with this apparatus some improvement in visual acuity occurred in all but 2, some better for near vision than distance and vice versa. Improvement occurred regardless of whether the patient had strabismic or anisometropic amblyopia. Two patients who were thought to have deprivation amblyopia both improved, but one had anisometropia and the other had anisometropia together with a squint. The former has been included in the anisometropic group and the latter in the strabismic group. It was noted that the majority of patients had nystagmoid movements in the amblyopic eye and also the crowding phenomenon. These patients did not respond so well to treatment. Fig. 3 gives the age distribution of the patients who were treated. Table 1 classifies the patients according to the type of deviation, associated ametropia, presence of nystagmoid movements, and eccentric fixation.

The results before and after treatment as assessed by visual acuity for distance and near are displayed in Figs. 4–6. In each of these figures acuity before treatment is plotted against acuity after treatment for distance (△) and near (▲) acuity. Patients who have not been previously treated are also indicated (▲⃝). According to this method of display the oblique sloping lines indicate no improvement after treatment and the extent to which the data are displaced upwards, that is towards the dashed line (6/6),

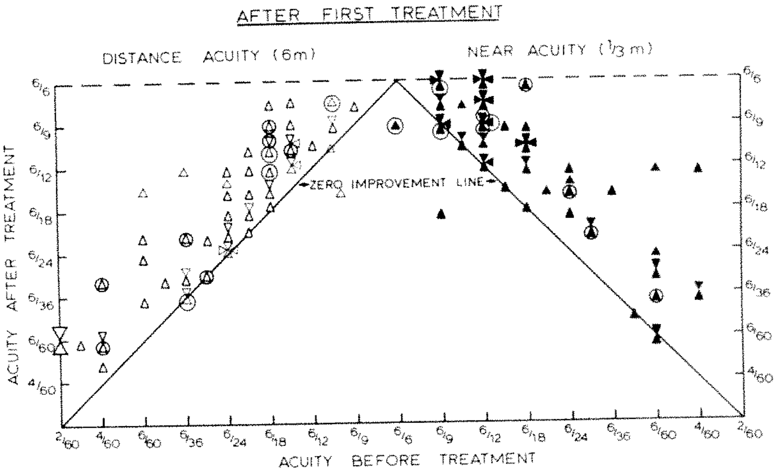

Fig. 4 *Improvement of distance (unfilled symbols) and near (filled symbols) acuity after the first 7 minutes of grating treatment. Enclosed symbols represent patients who have not had previous treatment. Upward displacement represents acuity improvement from treatment whereas data falling on the sloping lines represent no acuity change.*

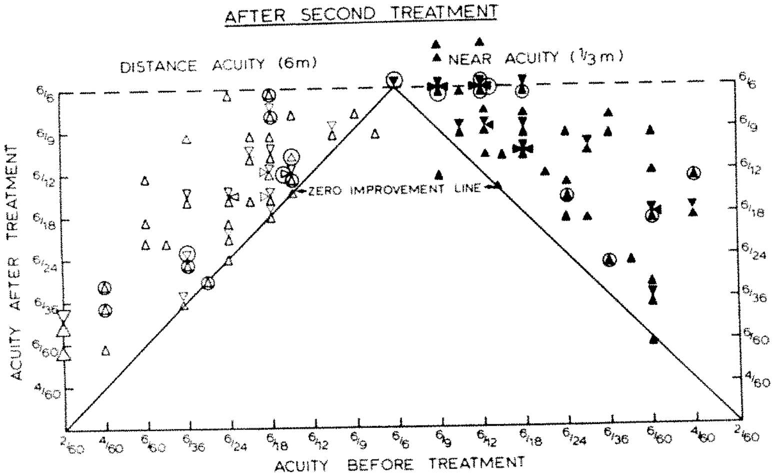

Fig. 5 *Improvement of distance (unfilled symbols) and near (filled symbols) acuity after the 7-minute treatment. Enclosed symbols represent patients who had not previously undertaken orthoptic treatment. Improvement of acuity (upward displacement) is with reference to acuity before any treatment (sloping line)*

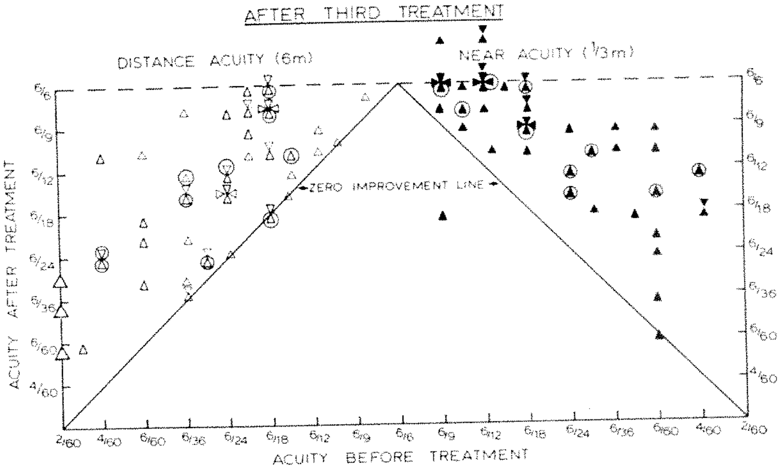

Fig. 6 *Improvement of distance (unfilled symbols) and near (filled symbols) acuity after the third 7-minute treatment. Enclosed symbols represent patients who had not previously undertaken orpthoptic treatment. Improvement of acuity (upward displacement) is with reference to acuity before any treatment (sloping lines)*

indicates the magnitude of the improvement with treatment compared with the original acuity before treatment. The results are displayed for the first 3 treatment sessions, each lasting 7 minutes. The data could have been displayed on other axes to amplify the large absolute improvement for low acuities, but it was decided to use this arbitrary but clinically familiar scale.

The results indicate that in the majority of cases acuity improved at both distance and near. As expected, cases which had not previously been treated with occlusion in one form or another improved more rapidly and to a greater extent with treatment. Improvement in acuity was maintained between treatments, and it is clear from the results that acuity improves in most cases across the 3 treatment sessions. After the third treatment session only 3 patients (7%) had failed to respond to treatment. The number of treatments required to achieve the maximum level of acuity by this new method varies considerably between patients. Even though some cases are slower than others to improve, the convenience and brevity of the treatment will still be economic in clinical time.

So far 22 patients have completed the treatment. The average number of treatments required to achieve the maximum visual acuity as 4 (see Table 2). Regression of visual acuity after treatment has been discontinued has never been more than one Snellen line and then only at 6 m. These patients have almost invariably had nystagmoid jerks of the amblyopic eye. The contrast thresholds for a low and medium frequency grating have remained stable even though letter acuity has varied.

The contrast threshold results also indicated improvement with treatment for both low and high spatial frequencies, which are known to be abnormal in this condition (Hess and Howell, 1977). In some cases contrast thresholds improved even though acuity was not measurably altered, indicating the more sensitive nature of the former measurement (Campbell and Green, 1965; Hess and Garner, 1977). In such cases subsequent treatments resulted in acuity as well as contrast threshold improvement.

To illustrate further that this new treatment technique improves *overall* visual function as well as acuity the contrast sensitivity function was measured in the laboratory for 1 patient aged 10 years before and after one 7-minute treatment session. Both the normal and fellow amblyope eyes were tested to ensure improvement did not result from experience with the technique. These results are displayed in Fig. 7 as spatial frequency versus contrast sensitivity for the normal ($\overset{\triangledown}{\circ}$) and fellow amblyopic ($\overset{\triangle}{\bullet}$) before (unfilled symbols) and after treatment (filled symbols). The results show that the contrast sensitivity abnormality for this patient is confined to only high spatial frequencies (type I amblyopia, see classification of Hess and Howell, 1977). The results show that treatment resulted in a substantial improvement in high-frequency contrast sensitivity of half a log unit, and grating acuity (extrapolation to axis) improved from 20 to 30 c/deg. Letter acuity improved from 6/24 to 6/9 for distance and from 6/18 to 6/9 for near vision. Since the normal eye acting as a control did not alter when contrast sensitivity was retested, it can be concluded that the improvement for the amblyopic eye resulted from treatment. Such visual improvement is dramatic when it is realised that treatment lasted for only 7 minutes and that contrast thresholds as well as acuity improved.

Figs. 8–10 represent three amblyopic patients chosen to represent the range of response from treatment. In the first case (Fig. 8) acuity for distance

Table 2 *Completed treatments*

Case No.	*Age (years)*	*Initial visual acuity*	*Final visual acuity*	*No. of 7-minute treatments required*
1	10	4/60	6/60×1	40
2	4 5/12	6/18	6/6	4
3	8	6/24	6/9+	6
4	6 10/12	6/18	6/9+	3
5	8 6/12	6/24	6/18	4
6	5 10/12	6/36	6/24	2
7	7 6/12	6/18+	6/9+	3
8	9	6/36+	6/9	26
9	9	6/12	6/12+	2
10	9 6/12	3/60	6/60	1
11	9 3/12	6/60	6/36	2
12	12	6/60	6/36+	3
13	8 6/12	6/9	6/6 –	1
14	10	6/60+	6/18	4
15	4 6/12	6/24+	6/6	3
16	6 6/12	6/18	6/9+	7
17	7 9/12	6/24+	6/6	2
18	9	6/24+	6/9	3
19	6 8/12	6/18+	6/6	8
20	10 2/12	6/24	6/18+	3
21	9	4/60	6/6	10
22	7 3/12	6/18+	6/9	5

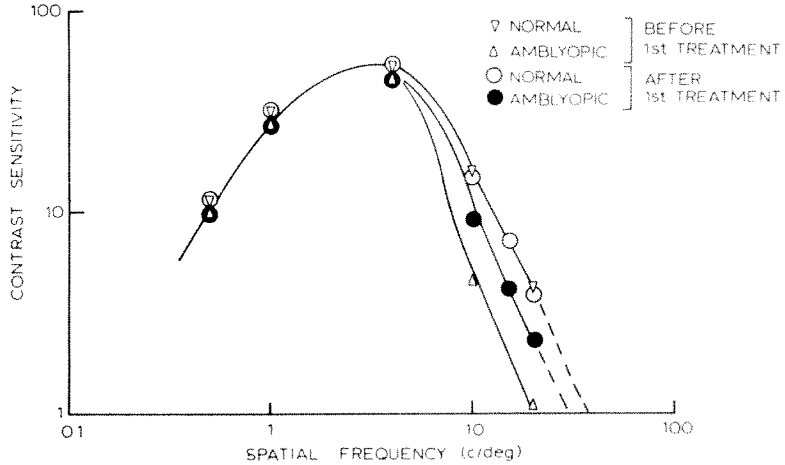

Fig. 7 *Contrast sensitivity functions are compared for the normal* (∇○) *and fellow amblyopic eye* (△●) *before and after* (0; ●) *7 minutes of treatment using gratings. Standard errors were never larger than the symbol size used*

and near vision improved from 4/60 to 6/6 after 10 treatment sessions (each of 7 minutes) spread over 21 days; this represents the largest magnitude improvement of any patient so far studied. Fig. 9 illustrates one of the most unsuccessful amblyopic patients in that acuity improved only from 6/36 (distance) and 6/24+ (near) to 6/12+ after 26 treatment sessions. The child was treated by the mother at home, and the sparsity of data is due to the infrequent visits for hospital assessment. One of the most rapid treatment effects is illustrated in Fig. 10, in which acuity of 6/18 improved to 6/6 after only 3 treatment sessions. The full case records for these three amblyopic cases are given elsewhere (Banks *et al.*, 1978).

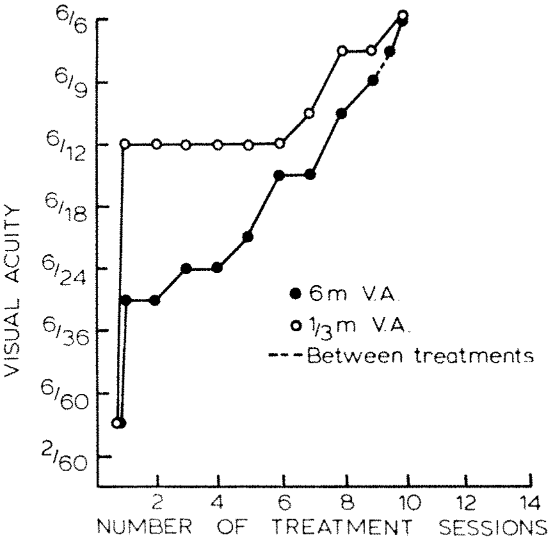

Fig. 8 *Case 1, age 9 years*

Discussion

While we consider this method to be a highly significant advance in the treatment of strabismic and anisometropic amblyopia, we believe there is a considerable danger (because of the treatment's effectiveness) that intractible diplopia could be induced, with all its disastrous and possibly medico-legal consequences if the treatment is applied inappropriately. Until more is known about the reason for the improvement in vision we consider that the use of this instrument should be confined to hospitals and clinics under strict clinical supervision.

The results of this study are important from 2 separate standpoints. Firstly, they indicate that this simplified and clinically convenient procedure is as effective as, if not more effective than, the currently used procedures, which are lengthy and psychologically disturbing. Secondly, such a result could have important underlying physiological implications, especially as in some cases the acuity and contrast sensitivity changes are large and extremely rapid.

The time course of these improvements and the age at which they occur do not tally in any simple manner with the numerous studies of the 'critical period' for visual deprivation in cats and monkeys (Wiesel and Hubel, 1963a, b; 1965a, b; van Noorden *et al.*, 1970; Blakemore and Van Sluyters, 1974). It is very unlikely that the amblyopes that we have studied have actually *lost* neurones which subsequently regenerate with treatment. It seems more probable, in the light of the treatment time course, that neurones in amblyopia have reduced function (Hess, 1977), resulting in depressed contrast sensitivity (Hess and Howell, 1977; see also Fig. 7).

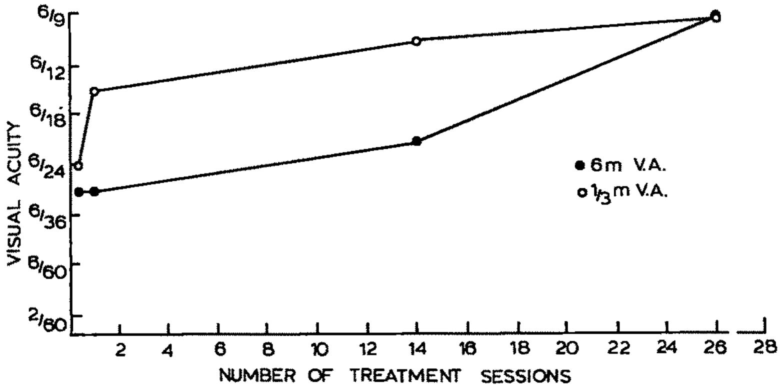

Fig. 9 *Case 2, age 9 years*

Yet a further possibility which has previously not been considered is that each neurone responds normally to its optimal stimulus but they do not work together as in normal vision, resulting in a scrambling of the transmitted signal. An analogy might be viewing a distant scene in the hot shimmering air of the desert, except of course it would not be moving and resemble that of a still photograph taken of the scene. Indeed we have made some preliminary observations on adult amblyopes whose contrast sensitivity measured with sine wave gratings is equal in the 2 eyes. However, the amblyope does not 'see' a regular periodic grating like the normal eye, for they describe it as being 'broken up' and 'jumbled' (Campbell *et al.*, in preparation). Neurophysiologists have not described such an anomaly, but this is because they have not looked for phase and orientational scrambling in the visual system of deprived animals.

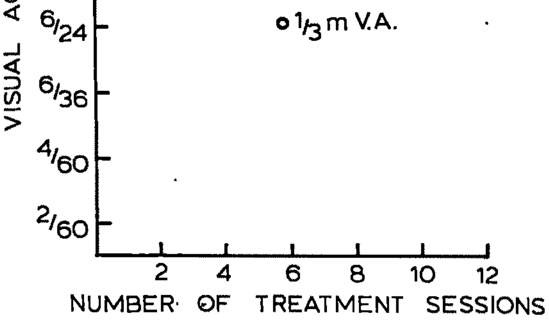

Fig. 10 *Case 3, age 6½ years*

A further analogy more familiar to the reader might be as follows. Imagine taking a short-duration flash photograph of an optotype test chart lying on the pebbles of a clear shallow stream. The resulting photograph would show multiple and complex (phase) distortions due to the rippling on the surface of the water. The resollable detail on the test type would be much less, though the integrated contrast between the black and white segments would remain constant. In other words, the amplitude information is maintained but the positional or phase information is corrupted.

In the conventional treatment of amblyopia by occlusion plenty of images are falling on the retina of the amblyopic eye as the child goes about its daily life; yet this input, while it improves vision slightly, does so very slowly and inadequately. What then is so special about a rotating grating? Adriana Fiorentini, of the University of Pisa, pointed out to us that nothing in the normal world rotates in this manner, nor does any movement of the body stimulate such movement on the retina. Perhaps the amblyopic visual system requires the whole gamut of motion?

We thank Mrs Fay Barnett and Miss Claire Smith, orthoptists of Addenbrooke's Hospital, and Dave Burr, of the physiological laboratory, for their help and discussion which contributed to this project. As always we are indebted to Clive Hood, without whose assistance this project would never have got off the ground. F. R. Hess was supported by a Rotary International Fellowship. We also wish to thank J. E. Cairns, FRCS, and J. Keast-Butler, FRCS, for providing suitable patients.

References

Banks, R. V., Campbell, F. W., and Hood, C. (1978). A neurophysiological approach to the treatment of amblyopia. *Journal of Physiology*, **275**, 16–17.

Banks, R. V., Campbell, F. W., Hess, R. F., and Watson, P. G. (1978). A new treatment for amblyopia. *British Journal of Orthoptics*, **35**, 1–12.

Blakemore, C., and Van Sluyters, R. (1974). Reversal of the physiological effects of monocular deprivation in kittens. Further evidence for a sensitive period. *Journal of Physiology*, **237**, 195–216.

Campbell, F. W. (1974). The transmission of spatial information through the visual system. *The Neurosciences Third Study Program*, pp. 95–103. MIT Press: London.

Campbell, F. W., Cleland, B., Cooper, G. F., and Enroth-Cugell, C. (1968). The angular selectivity of visual cortical cells to moving gratings. *Journal of Physiology*, **198**, 237–250.

Campbell, F. W., Cooper, G. F., and Enroth-Cugell, C. (1969). The spatial selectivity of visual cells of the cat. *Journal of Physiology*, **203**, 223–235.

Campbell, F. W., and Green, D. G. (1965). Monocular versus binocular visual acuity. *Nature*, **208**, 191–192.

Catford, G. V. (1967). *Transactions of the Ophthalmological Societies of the United Kingdom*, **87**, 179.

Chavasse, F. B. (1939) .*Worth's Squint*, 7th edn., p. 437. Ballière, Tindall & Cox: London.

Dayson, A. (1968). Five year survey of the use of occlusion in the treatment of eccentric fixation. *British Journal of Orthoptics*, **25**, 66.

Buffon, G. Leclerc de (1746). Dissertation sur les causes du strabisme, ou des yeux louches. *Mémoires de l'Académie Royale des Sciences* (Paris), pp. 231–248.

Granit, R. (1974). The concept of receptive field. *Documenta Ophthalmological Proceedings* Series XIth ISCERG Symposium, p. 3.

Granit, R. (1977). The purposive brain, p. 130. MIT Press: Cambridge, Mass.

Gstalder, R. J., and Green, D. G. (1971). Laser interference acuity in amblyopia. *Journal of Pediatric Ophthalmology*, **8**, 251–255.

Hess, R. F. (1971). An appraisal of the prognosis and treatment for a functional curve of horizontal concomitant strabismus. *Australian Journal of Optometry*, **54**, 129–148.

Hess, R. F., and Garner, L. F. (1977). The effect of corneal edema on visual function. *Investigative Ophthalmology*, **16**, 5–13.

Hess, R. F. (1977). Assessment of stimulus field size for strabismic amblyopes. *American Journal of Optometry and Physiological Optics*, **54**, 292–299.

Hess, R. F., and Howell, E. R. (1977). The threshold contrast sensitivity function in strabismic amblyopia: evidence for a two type classification. *Vision Research*, **17**, 1049–1057.

Levi, D. M., and Harwerth, R. S. (1977). Spatio-temporal interactions in anisometropic and strabismic amblyopia. *Investigative Ophthalmology*, **16**, 90–95.

Maffei, L., and Fiorentini, A. (1973). The visual cortex as a spatial frequency analyser. *Vision Research*, **13**, 1255–1267.

Oliver, M., and Nawratzki, I. (1971). Screening of preschool children for ocular anomalies. II. Amblyopia: Prevalence and therapeutic results at different ages. *British Journal of Ophthalmology*, **55**, 467.

Piligrim, A., and Turner, S. (1974). A survey of cases of eccentric fixation in children up to 10 years of age, seen during the last 10 years. *British Journal of Orthoptics*, **31**, 59.

Pope, L. G. (1971). Treatment of eccentric fixation without occlusion. *British Journal of Orthoptics*, **28**, 77.

Robson, J. G. (1975). Receptive fields: Neural representation of the spatial and intensive attributes of the visual image. *Handbook of Perception*, vol. 5, p. 81. Edited by E. C. Carterette and M. P. Friedman. Academic Press: London.

van Noorden, G. K., Dowling, J. E., and Ferguson, D. C. (1970). Experimental amblyopia in monkeys. *American Archives of Ophthalmology*, **84**, 206–214.

Wiesel, T. N., and Hubel, D. H. (1963a). Effects of visual deprivation on morphology and physiology of cells in the cat lateral geniculate body. *Journal of Neurophysiology*, **26**, 978–993.

Wiesel, T. N., and Hubel, D. H. (1963b). Single cell responses in striate cortex of kittens deprived of vision in one eye. *Journal of Neurophysiology*, **26**, 1003–1017.

Wiesel, T. N., and Hubel, D. H. (1965a). Comparison of the effects of unilateral and bilateral eye closure on cortical unit responses in kittens. *Journal of Neurophysiology*, **28**, 1029–1040.

Wiesel, T. N., and Hubel, D. H. (1965b). Extent of recovery from effects of visual deprivation in kittens. *Journal of Neurophysiology*, **28**, 1040–1060.

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Stereopsis and spatial perception in amblyopes and uncorrected ametropes

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SUMMARY Amblyopes and nonamblyopes were compared on 2 tests of spatial perception. One, the Titmus stereotest, provided only disparity cues and thus measured pure stereopsis. The other, the 3-rods test, provided a variety of monocular and binocular cues and measured the precision of distance discrimination. On both tests the amblyopes were significantly worse than nonamblyopes with equivalent acuity deficits. The Titmus stereotest was found to be an effective means of screening for amblyopia. The results of the distance discrimination test are discussed in terms of their clinical and physiological implications.

Perception of three-dimensional space is facilitated by a number of cues, such as accommodation, convergence (Lie, 1965), movement parallax (Johannson, 1973), apparent size, shape, overlay, perspective, and illumination gradients. In addition to these monocular cues species with overlapping visual fields can utilise the disparity information provided by the horizontal separation between their 2 eyes. A single point in space is imaged at 2 disparate points on the 2 retinae (unless it is being fixated), and the degree of disparity between the 2 retinal points is dependent on the spatial location of the point. In this paper 'depth perception' is used to refer to perception utilising any number of the cues mentioned above, and 'stereopsis' is reserved for perception of depth arising solely from disparity information. Thus stereopsis can be assessed only when all other cues have been eliminated, whereas depth perception can be assessed when any number of cues are present.

In the last 10 years considerable advances have been made in our knowledge of the neurophysiological basis of stereopsis. Cortical cells which are tuned to respond maximally to specific retinal disparities have been found in cats (Barlow *et al.*, 1967) and sheep (Clarke *et al.*, 1976). This specificity is present at birth in some species but not others; it has been found in sheep (Ramachandran *et al.*, 1977) but not in cats (Pettigrew, 1974). There is evidence that normal visual experience is essential for the development of these disparity detector cells. In cats the specificity and binocularity of these cells can be considerably reduced by monocular deprivation during a 'critical period' which lasts from birth to 3 months (Hubel and Wiesel, 1970; Blakemore, 1976). In sheep cell specificity is present at birth, but it has been suggested (Ramachandran *et al.*, 1977) that normal visual experience is required to enhance the binocularity of the disparity detector cells, which at birth respond to monocular stimulation.

The abundance of evidence from visual deprivation experiments on animals may parallel clinical evidence from man, in whom a monocular optical or muscular defect in early childhood precedes amblyopia. This condition is characterised by the inability of the defective eye to achieve a high visual acuity unless the causative defects are corrected before the end of a critical period. It has been suggested that, for man, this extends from birth to the end of the third year (Banks *et al.*, 1975). Similar monocular defects occurring later in life do not give rise to amblyopia.

Another characteristic of amblyopes is their failure to perceive depth in tests of stereopsis which provide only disparity cues (Frisby *et al.*, 1975; Reinecke and Simons, 1974; Walraven, 1975). It seems possible that they, like the experimental animals already described, lack cortical disparity detector cells, because they did not receive appropriate visual stimulation during childhood.

If amblyopes do not perceive disparity as a cue to spatial location, they must either make use of other cues or perceive the world as being two-dimensional. This study was designed to investigate these possibilities. The perceptual skills of amblyopes and nonamblyopes were compared in a task which offered cues other than disparity to aid spatial

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localisation. These additional cues included monocular cues, such as apparent size changes and luminance changes, and binocular cues such as accommodation and convegence. In addition visual acuity and stereopsis were measured in order to evaluate their contributions to spatial perception.

Methods

Subjects were selected from a population of approximately 200 undergraduates who were screened on a Snellen letter chart at 6 m. All those who achieved unequal right-eye and left-eye acuities were refracted and examined ophthalmoscopically, and relevant details of ocular history were recorded.

Amblyopes were defined as those who could not achieve equal acuities when wearing full optical corrections. Nonamblyopes could all achieve equal acuities of 6/6 or better after full optical correction. Eight amblyopes were found (7 anisometropic and 1 strabismic) none of whom had eccentric fixation by visuscopy. This proportion (4%) is close to the incidence of amblyopia reported by other authors, for example, Sutcliffe (1960).

Sixteen nonamblyopes selected as controls were either uncorrected or undercorrected myopes or astigmats. None of them had worn their full optical corrections for at least 5 years, and they were selected on the assumption that they, like the amblyopes, would have adapted to their acuity deficits. Eight of these control nonamblyopes were selected as subjects because their acuities in both eyes closely matched the acuities of the 8 amblyopes. The other 8 control nonamblyopes were chosen because their acuities covered a wide range which would be useful in correlative procedures.

Each of the 24 subjects performed the following tests: (1) Snellen acuity test; (2) Titmus test of stereoacuity; (3) 3-rods test of depth discrimination. Half the subjects (4 amblyopes and 8 nonamblyopes) were used in an additional experiment (4) to investigate the importance of luminance as a cue in the 3-rods test.

MEASUREMENT OF VISUAL ACUITY

Visual acuities were measured monocularly on a standard Snellen chart at 6 m. Acuity was recorded as the last line read faultlessly. Snellen fractions were converted to angular subtense in minutes of arc in accordance with the conventional rule that the angle subtended by a single element of the Snellen letter represents the resolution threshold. Thus 6/6 is equivalent to a resolution of 1 minute of arc.

MEASUREMENT OF STEREOACUITY

Stereoacuity can be defined as a quantitative measure of stereopsis. It was assessed using the Titmus stereotest (Titmus Optical Co. Inc., Petersburg, Virginia). Subjects wore a pair of spectacles carrying 2 mutually perpendicular Polaroid lenses which dissociated the 2 eyes. The Titmus test stimuli consisted of 10 pairs of orthogonally polarised images, so that only 1 of the pair was seen by each eye. There was a small horizontal disparity between the 2 images in each pair, and in the presence of stereopsis this disparity cue was interpreted as a depth cue. Ten different degrees of disparity were presented in the 10 test stimuli. Each stimulus (that is, pair of images) showed a cluster of 4 rings. Only 1 of the 4 included the disparity cue, which made the ring appear to stand above the plane of the background if stereopsis was present. Subjects were required to make a forced choice response to report the location of the raised ring in relation to the cluster for each of the 10 stimuli. Stereoacuity was recorded as the smallest disparity correctly interpreted as a depth cue.

MEASUREMENT OF DEPTH DISCRIMINATION

Depth discrimination was measured by the three rods test (Helmholtz, 1866). The apparatus is shown and described in Fig. 1.

In designing the 3-rods apparatus it became apparent that the central rod's position along the sagittal axis determined its luminance: as it approached the front of the box, where the light source was situated, it appeared brighter. This cue could be utilised in making alignments by matching the luminance of the mobile central rod to that of the 2 fixed rods.

To assess the effect of this cue 12 subjects performed the 3-rods test twice on 2 slightly different versions of the apparatus. One version was exactly as described in Fig. 1. The other had all interior surfaces of the box painted black; this reduced the amount of internal reflection from walls and maximised the directionality of illumination within the box.

Subjects were seated 6 m away from the apparatus with instructions to keep as still as possible, so that the motion parallax cue was minimised. For each trial the subject was required to align the central mobile rod with the 2 fixed rods twice. The first alignment was made by pulling the rod forwards with a single smooth movement. The position of the pointer was then recorded by the experimenter, and the subject was instructed to prepare for the second alignment by pulling the central rod right up to the front of the box. The second alignment was made by allowing the rod to regress under the weight of the pulley system, again with a single smooth movement. The new position of the pointer was recorded, and the subject was instructed to prepare for the next trial by allowing the rod to return to the back of the box. No time constraints were imposed on the trials. Pointer positions were recorded as errors in millimetres (that is, distance from the correct alignment position). Six trials (pairs of alignments) were made in each of 4 conditions in the following order:

Condition 1=both eyes open, room lights on (luminance 4·5 foot-lamberts). Condition 2=only right eye open, room lights on (luminance 4·5 foot-lamberts). Condition 3=only left eye open, room lights on (luminance 4·5 foot-lamberts). Condition 4=both eyes open, room lights off (luminance 0·01 foot-lamberts). Thus each subject made a total of 48 alignments.

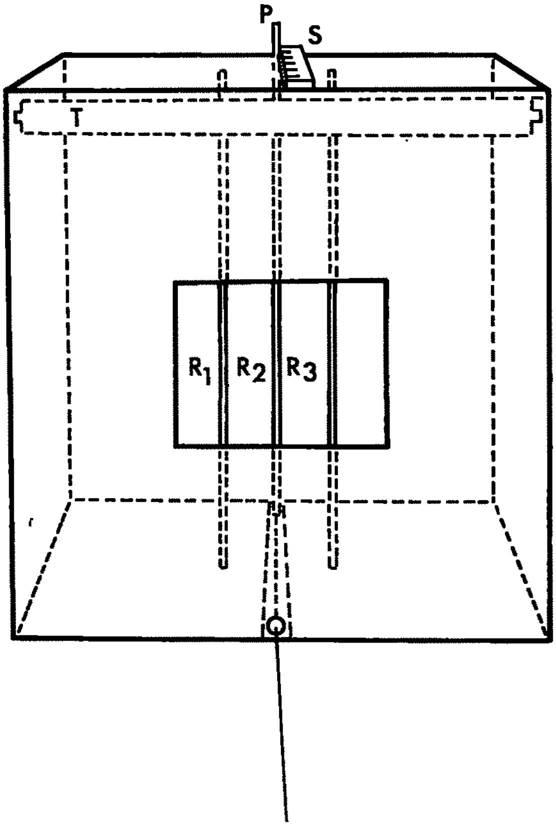

Fig. 1 *Apparatus used to measure depth discrimination: 3-rods test. The two outer white rods (R1 and R3) were fixed inside the black box (50×50×70 cm) and the central white rod (R2) was free to travel sagittally in a groove in the base of the box. The position of the central rod was indicated by the pointer (P) attached to it which protruded through a slit in the top of the box. A millimetre scale (S) lay along the slit so that the position of the pointer could be precisely recorded. The box was internally illuminated by a fluorescent tube (T) in the upper front corner. All interior surfaces were painted white except the back wall, which was black, in order to provide a background against which the white rods could be seen. The mobile central rod was attached to a pulley system such that it could either be pulled forward by a subject, or allowed to slide backwards under the weight of the pulley system. The diagram shows the subject's view of the apparatus. The ends of the 3 rods were not visible through the rectangular frontal aperture at any time*

Results

VISUAL ACUITY AND STEREOACUITY

Table 1 shows visual acuities in minutes of arc and Titmus stereoacuities in seconds of arc for all subjects. The 3 columns distinguish (1) amblyopes, (2) nonamblyopes with acuities closely matched to those of the amblyopes, and (3) other nonamblyopes. Adjacent subjects in columns 1 and 2 were treated as matched pairs for statistical purposes.

Amblyopes were significantly worse than nonamblyopes on the Titmus stereotest (t=3·59, P<0·005).

Fig. 2 shows the relationship between Snellen acuity of worse eye and Titmus stereoacuity.

All amblyopes failed to perceive any of the Titmus test stimuli in depth, as did one strabismic nonamblyope (24). Uncorrected myopic nonamblyopes performed well, scoring the maximum stereoacuity available. Uncorrected astigmatic nonamblyopes fell between the 2 extremes, and there is some indication that their stereoacuity correlated with their worse-eye-acuity. The dotted line in Fig. 2 indicates this correlation approximately. Quantitative evaluation is not justified in view of the small sample size.

DISTANCE DISCRIMINATION MEASURED BY THE 3-RODS TEST

Table 2 shows the errors (in centimetres) made by each subject on the white painted 3-rods apparatus. Subjects are arranged in 3 groups as in Table 1. The first 4 columns of error scores in each group's data show the means of errors made in the 12 trials in each of the 4 conditions. These are numbered 1 to 4, as in 'Methods'. The last 2 columns for each group show the means of errors made in all 48 trials. Fig. 3 shows the errors made by the 12 subjects who were tested on both the black painted and the white painted 3-rods apparatus. Errors were significantly greater on the white painted apparatus (t=3·04, P=0·01).

Better eye performance was compared with worse eye performance (conditions 2 and 3). The worse eye tended to make larger errors than the better

Table 1 *Visual acuities and stereoacuities for all subjects*

Amblyopes				*Acuity-matched nonamblyopes*				*Other nonamblyopes*			
Subject no.	*Snellen acuity of better eye (min arc)*	*Snellen acuity of worse eye (min arc)*	*Titmus stereoacuity (sec arc)*	*Subject no.*	*Snellen acuity of better eye (min arc)*	*Snellen acuity of worse eye (min arc)*	*Titmus stereoacuity (sec arc)*	*Subject no.*	*Snellen acuity of better eye (min arc)*	*Snellen acuity of worse eye (min arc)*	*Titmus stereoacuity (sec arc)*
1	0·67	1·5	> 1000	9	0·67	2·0	40	17	0·67	0·83	40
2	0·67	1·5	40	10	0·67	1·5	40	18	0·67	1·0	60
3	0·67	3·0	> 1000	11	0·67	4·0	40	19	0·67	1·0	40
4	0·83	1·0	400	12	0·83	1·0	40	20	1·0	4·0	60
5	0·83	1·5	800	13	0·83	1·0	40	21	1·0	1·0	40
6	0·83	2·0	800	14	0·83	2·0	40	22	1·0	1·0	80
7	1·5	2·0	> 1000	15	1·0	1·5	60	23	1·0	2·0	200
8	1·5	3·0	400	16	1·0	2·0	40	24	1·5	20·0	> 1000

eye, but the difference was not significant (t=0·99, P=0·2). The correlation between acuity and monocular performance was also found to be insignificant (better eye, r=0·074; worse eye, r=0·117). The possibility that the level of room illumination provided a luminance cue was assessed by comparing performances in conditions 1 and 4; they were not significantly different (t=0·009, P$\geqslant$0·3).

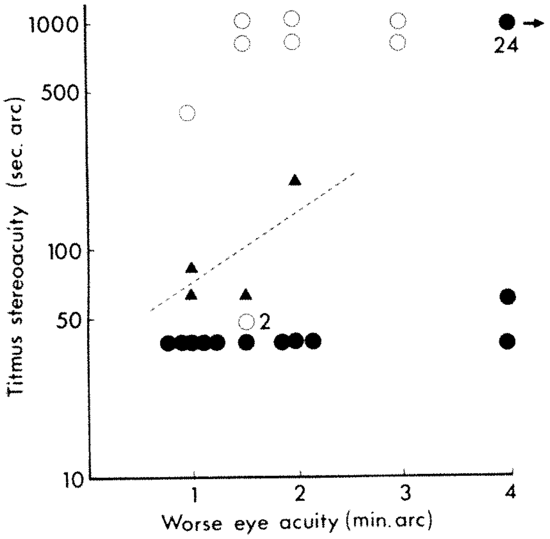

Fig. 2 *Comparison of Snellen acuity of worse eye with Titmus stereo-acuity.* ● = *uncorrected myopic nonamblyopes.* ▲ = *uncorrected astigmatic nonamblyopes.* ○ = *amblyopes. 24 = a nonamblyope with alternating esotropia. 2 = a subject who was classified as an amblyope by the acuity criterion (see 'Methods'). She later obtained a contact lens correction for irregular astigmatism which equalised her acuities; thus her original classification was shown to be wrong*

Each subject's better binocular performance was compared with his better monocular performance (condition 1 or 4 compared with 2 or 3). Errors in centimetres are shown in Fig. 4.

Binocularity improved performance significantly for amblyopes (t=16·53, P<0·005) and for nonamblyopes (t=2·15, P=0·25). The amount of improvement from binocularity, that is, the reduction in error, was calculated for amblyopes and their acuity-matched nonamblyopic counterparts. A comparison of these improvement scores showed no significant differences (t=0·79, P=0·25).

Fig. 5 shows the error scores of amblyopes and their acuity-matched nonamblyopic counterparts. Amblyopes' errors were significantly greater (t=2·39, P=0·025).

Discussion

Two perceptual capacities have been measured: distance discrimination when several cues are presented, and stereopsis when all cues except disparity are eliminated. Neither of these capacities was found to be simply determined by visual acuity, and yet both capacities were significantly reduced in amblyopes (Figs. 2 and 5). Before considering the implications of these 2 findings the results will be examined in greater detail.

VISUAL ACUITY AND STEREOACUITY

The inability of amblyopes and strabismics to perceive the disparity cues in the Titmus stereotest (Fig. 2) has been shown previously (Reinecke and Simons, 1974). A correlation between visual acuity and stereoacuity has also been previously reported

Table 2 *Results of the 3-rods test of distance discrimination. Mean errors (in cm) for each of the 4 test conditions (as defined under 'Methods') and overall conditions are shown for each subject. Subjects are listed in the same order as in Table 1*

Amblyopes						*Nonamblyopic acuity matches*						*Nonamblyopes*					
Three-rods test errors (mean of 12 trials for each condition in cm)				*Mean of 48 trials (cm)*	*Mean of 48 trials (sec arc)*	*Three-rods test errors (mean of 12 trials for each condition in cm)*				*Mean of 48 trials (cm)*	*Mean of 48 trials (sec arc)*	*Three-rods test errors (mean of 12 trials for each condition in cm)*				*Mean of 48 trials (cm)*	*Mean of 48 trials (sec arc)*
C.1	*C.2*	*C.3*	*C.4**			*C.1*	*C.2*	*C.3*	*C.4*			*C.1*	*C.2*	*C.3*	*C.4*		
11·70	12·30	10·07	8·89	10·74	36·5	2·11	4·73	3·22	1·18	2·81	9·6	2·77	2·84	2·74	3·07	2·86	9·7
0·93	5·49	5·53	1·18	3·28	11·2	2·27	3·04	3·05	3·46	2·96	10·1	3·09	4·64	9·24	4·23	5·03	17·1
3·65	5·86	4·84	3·95	4·58	15·6	2·11	6·37	1·97	4·23	3·67	12·5	2·36	2·43	3·18	2·04	2·49	8·5
2·33	3·43	4·83	4·36	3·74	12·7	2·29	4·21	5·09	3·01	3·65	12·4	7·38	2·29	5·63	4·83	5·03	17·1
4·49	6·18	7·76	4·98	5·85	19·9	6·23	7·28	6·48	3·88	6·00	20·4	7·18	7·10	14·94	4·60	8·46	28·8
5·39	9·15	7·68	2·44	6·17	21·0	0·71	1·76	2·75	1·95	1·79	6·1	1·27	3·86	5·37	1·80	3·09	10·5
5·07	6·26	7·52	6·15	6·25	21·3	2·23	4·10	4·70	1·80	3·21	10·9	3·13	4·39	3·95	2·00	3·37	11·5
5·11	5·98	5·96	2·44	4·87	16·6	2·13	3·65	1·53	3·62	2·73	9·3	3·73	2·24	3·39	4·10	3·37	11·5

*Conditions 1, 2, 3, and 4 (see text)

(Levy and Glick, 1974), but the high performance of the nonamblyopic myopes appears to conflict with this correlation. However, it can be explained by the fact that the Titmus test was conducted at a distance of 30 cm; at this distance myopia of less than 3 DS would have no effect on visual acuity. None of the nonamblyopic myopes exceeded this 3 DS limit.

DISTANCE DISCRIMINATION

Fig. 3 shows that luminance was an important cue facilitating precision in the black painted 3-rods apparatus. Increasing the internal reflections by painting the interior surfaces white reduced this cue considerably, and precision of alignment was correspondingly worse. Binocularity proved to be of considerable advantage to all subjects (Fig. 4). Some of the improvement attained with binocularity can be attributed to the retinal disparity cue, but this explanation is applicable only in the case of nonamblyopic subjects. Amblyopic subjects were unable to perceive any of the disparity cues in the Titmus stereotest, and so it seems unlikely that they could make use of them in the 3-rods test when the angular disparities were much smaller. Amblyopes must therefore have made use of other cues provided by binocularity, for example, proprioceptive information from accommodation and convergence.

COMPARISON OF STEREOPSIS AND DISTANCE DISCRIMINATION

Fig. 6 shows the relationship between distance discrimination measured as angular errors on the 3-rods test and Titmus stereoacuity measured as angular disparities detected. All subjects made smaller errors on the 3-rods test than their performance on the Titmus stereotest would have predicted. Hence all points lie to the right of the dotted line, which represents equivalent disparities on the 2 tests. The presence of cues additional to disparity must account for this finding. The horizontal

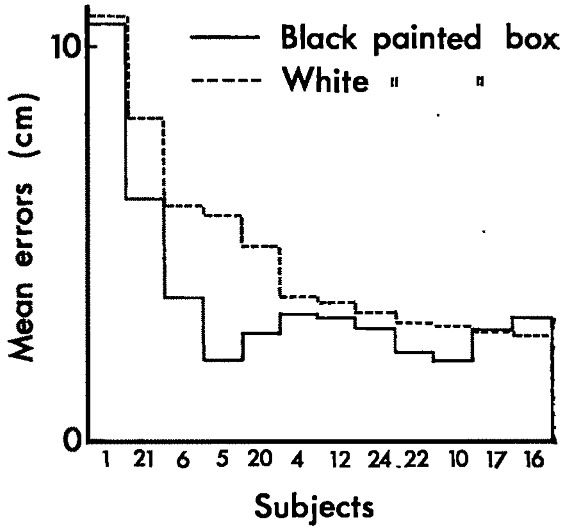

Fig. 3 *Comparison of performance on the black painted 3-rods apparatus with performance on the white painted version. Mean errors over all 48 trials are shown for 12 subjects*

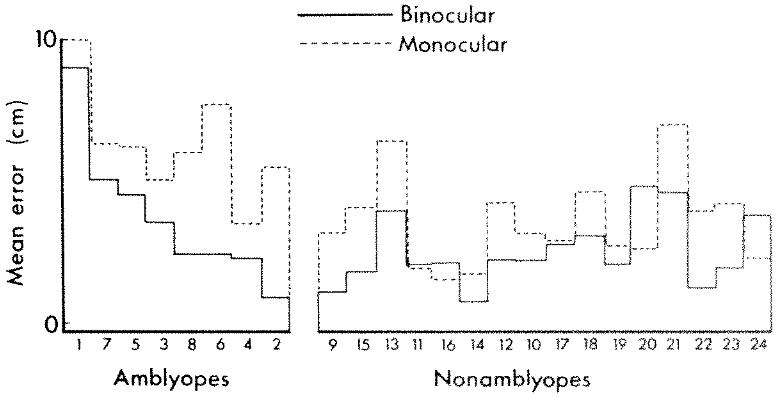

Fig. 4 *Comparison of monocular performance with binocular performance for each subject. The solid lines show each subject's smaller binocular error (that is, performance in condition 1 or 4). The dotted lines show smaller monocular error (that is, performance in condition 2 or 3)*

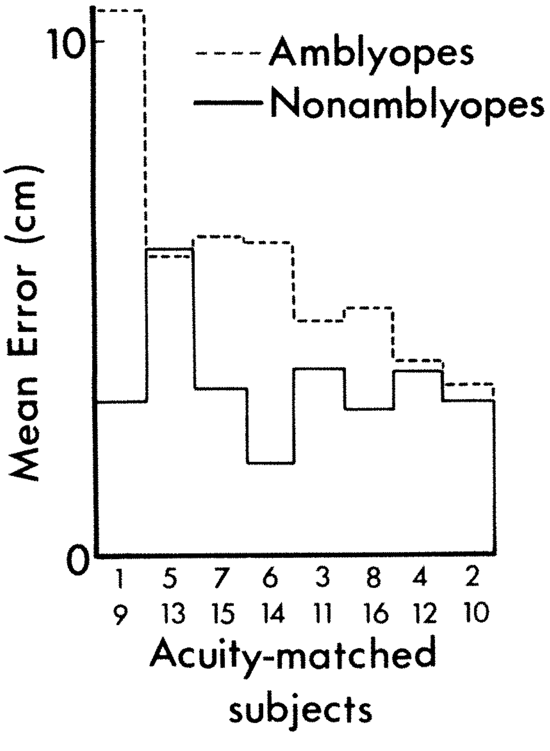

Fig. 5 *Comparison of amblyopes with acuity-matched nonamblyopes. Mean errors over all 48 trials on the white painted apparatus are plotted for acuity-matched pairs of amblyopes and nonamblyopes*

separation between amblyopes and nonamblyopes corresponds to the vertical separation between them in Fig. 2.

CLINICAL IMPLICATIONS

The value of the Titmus test as a method for detecting amblyopia and strabismus has been confirmed. The 3-rods test, on the other hand, provides more descriptive information about the perceptual abilities of subjects in an environment offering a variety of spatial cues. The Titmus test provides a pure measure of stereopsis, whereas the 3-rods test measures the precision of spatial perception in functional terms.

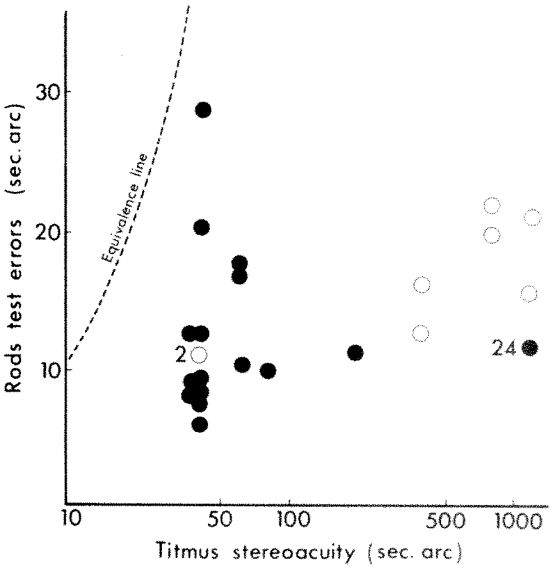

Fig. 6 *Comparison of results obtained from 2 tests of spatial perception. Errors made on the 3-rods test of distance discrimination are plotted vertically on a linear scale of angular subtense in seconds of arc. Disparities just detected on the Titmus stereotest are plotted horizontally on a logarithmic scale of angular subtense in seconds of arc. The dotted line shows the locus of equivalent angular scores.* ○ = *amblyopes.* ● = *non-amblyopes. 2 and 24 are explained in Fig. 2*

The amblyopic group's mean error of 5 cm at a testing distance of 6 m corresponds to an error of 15 yd (14 m) at a mile. This represents an order of accuracy which is adequate for most perceptual tasks normally encountered, with the exception of those in which high speed or unusual surroundings necessitate greater precision. The results of the 3-rods test confirm that, despite their lack of stereopsis, the perceptual world of amblyopes is definitely three-dimensional.

PHYSIOLOGICAL IMPLICATIONS

Lack of stereopsis has been attributed to the absence of the cortical disparity detection mechanism (Blakemore and van Sluyters, 1974). Various animal studies have shown that abnormal early visual experience can cause changes in the binocularity of cortical function. Amblyopes and strabismics suffer abnormal early visual experience as a result of their optical or muscular defects, and they have been shown, by performance of the Titmus test, to lack stereopsis based on disparity detection alone. Thus it seems possible that they lack binocular function at a cortical level. However, their ability to benefit from binocularity in the 3-rods test (Fig. 4) suggests that they may retain proprioceptive functions mediated by accommodation and convergence. The pathways involved in these proprioceptive functions are not known.

Hochberg (1972) reviewed studies of accommodation and convergence as spatial cues and concluded that they are usually extremely weak cues. Perhaps amblyopes learn to make better use of them in order to compensate for their inability to detect disparity cues. This possibility could be investigated by comparing amblyopes and acuity-matched non-amblyopes on a task presenting only proprioceptive information. Such a comparison would also provide some information about the pathways of proprioception.

References

Banks, M. S., Aslin, R. N., and Letson, R. D. (1975). Sensitive period for the development of human binocular vision. *Science*, **190**, 675–677.

Barlow, H. B., Blakemore, C., and Pettigrew, J. D. (1967). The neural mechanism of binocular depth perception. *Journal of Physiology*, **193**, 327–342.

Blakemore, C. (1976). The conditions required for the maintenance of binocularity in the kitten's visual cortex. *Journal of Physiology*, **261**, 432–444.

Blakemore, C., and van Sluyters, R. C. (1974). Experimental analysis of amblyopia and strabismus. *British Journal of Ophthalmology*, **58**, 176–182.

Clarke, P. G. H., Donaldson, L. M. L., and Whitteridge, D. (1976). Binocular visual mechanisms in cortical areas 1 and 2 of the sheep. *Journal of Physiology*, **256**, 509–526.

Frisby, J. P., Mein, J., Saye, A., and Stanworth, A. (1975). Use of random-dot stereograms in the clinical assessment of strabismic patients. *British Journal of Ophthalmology*, **59**, 545–552.

Helmholtz, H. (1896). Die einfachen Farben. In *Handbuch der physiologischen Optik*, vol. 2, p. 306. Edited by J. P. C. Southall. Dover Publications Inc.

Hochberg, J. (1972). Visual depth perception. In *Woodworth and Schlosberg's Experimental Psychology*, pp. 477–480. Edited by J. W. Kling and L. A. Riggs. Methuen: London.

Hubel, D. H., and Wiesel, T. N. (1970). The period of susceptibility to the physiological effects of unilateral eye closure in kittens. *Journal of Physiology*, **206**, 419–436.

Johansson, G. (1973). Monocular movement parallax and near-space perception. *Perception*, **2**, 135–146.

Levy, B. S., and Glick, E. B. (1974). Stereoscopic perception and Snellen visual acuity. *American Journal of Ophthalmology*, **78**, 722–724.

Lie, I. (1965). Convergence as a cue to perceived size and distance. *Scandinavian Journal of Psychology*, **6**, 109–116.

Pettigrew, J. D. (1974). The effect of visual experience on the development of stimulus specificity by kitten cortical neurones. *Journal of Physiology*, **237**, 49–74.

Ramachandran, V. S., Clarke, P. G. H., and Whitteridge, D. (1977). Cells selective to binocular disparity in the cortex of newborn lambs. *Nature*, **268**, 333–335.

Reinecke, R. D., and Simons, K. (1974). A new stereoscopic test for amblyopia screening. *American Journal of Ophthalmology*, **78**, 714–721.

Sutcliffe, S. (1960). Visual screening of three year old children. *British Orthoptic Journal*, **17**, 1–11.

Walraven, P. L. (1975). Amblyopia screening with random dot stereograms. *American Journal of Ophthalmology*, **80**, 893–900.

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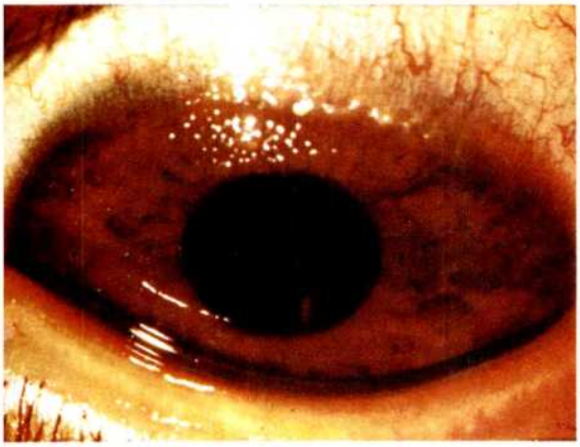
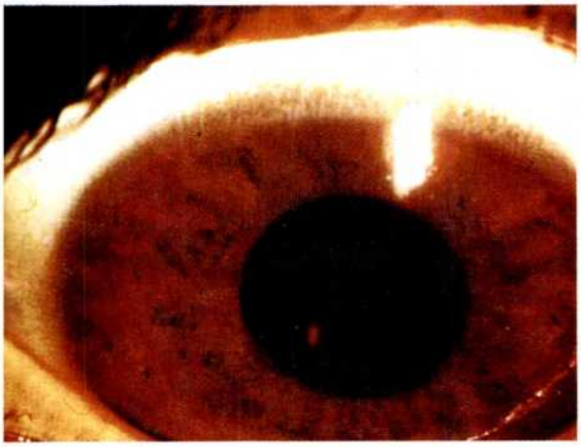


he superior limbus in a placebo treated eye of a patient suffering from nal kerato-conjunctivitis, stained with fluorescein. Note the limbal eraemia and swelling and the irregularity of the corneal surface.



he opposite eye of the same patient treated with sodium cromoglycate drops. Before treatment, both eyes appeared similar.

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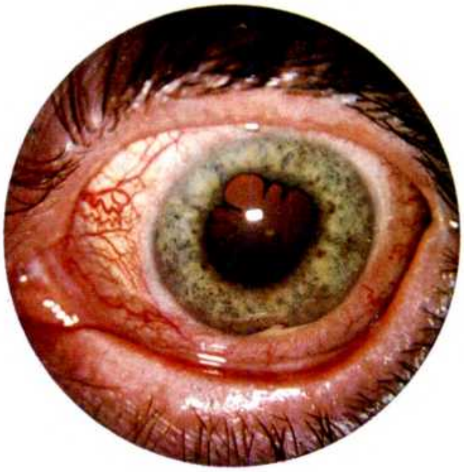

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British Journal of Ophthalmology, 1978, **62**, 763–764

Pseudostrabismus: an audit

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SUMMARY 331 children presenting with pseudostrabismus were assessed retrospectively; 24% of 77 ametropes developed a true convergent squint. Only 1·65% of 243 emmetropes developed a true squint, an incidence much less than in an unselected group. A close follow-up of emmetropic children presenting with pseudostrabismus would seem to be unjustified.

A perpetual problem in ophthalmology is an outpatient load of trivia mixed with other conditions that really need skilled attention. The excessive time spent on trivial cases leads to a consideration of methods of reducing the overload. Pseudostrabismus is a field in which limitation of the supervision of attenders who would be no worse off without such supervision seems to be a promising line of investigation.

It may be said that little time is wasted in supervising children with this condition, as a surgeon may take only a minute or two to examine a cooperative child but much longer if the child is fractious. Additionally, it takes further time for the patient and his mother to get in and out of the consulting room, and when the orthoptist takes over an even more liberal period is allowed for the examination. Probably of more importance is that the time spent by the surgeon and the orthoptist at each visit is small compared with that spent by the patient and his parent or parents, together on occasions with other siblings. In the clinics from which this study derives it would be reasonable to guess that the average patient waits up to 45 minutes to be seen and may spend 2 hours or so coming and returning home.

The foregoing considerations have led to a retrieval of clinical material from routine case notes to work out figures that would show either that time is wasted in the surveillance of pseudostrabismus or that the incidence of the subsequent development of squint demanding treatment actually justifies the time spent on such patients.

The reported incidence of true squint in the general population of children varies. Worth and Chavasse (1959) gave a range of 2 to 5% quoting Thomson in Glasgow, McNeil, and MacQueen and Sutherland, all of whom reported on varying incidences ranging from 2·7% to 7·2% in groups of children living in Scotland. Pratt-Johnson and Lunn (1967) in Canada found an incidence of 4·5% of 6-year-olds, and Graham (1974) in a more recent study conducted by trained observers in Cardiff found an incidence of 5·6%. An estimate of the incidence of squint in the West Sussex Area whence the present study derives is 3·9%, but it is thought that there are an additional 1 to 2% of affected children who had squints that have been controlled. This brings the total figure up to about 5·5%, which is near the national norm.

Of new patients presenting with convergent squint in our orthoptic departments during the calendar years 1975 and 1976 62·5% showed no sign of a squint.

Patients and methods

This retrospective survey concerns 331 patients in whom the criteria for inclusion were: (1) A presenting history of convergent squint, or just squint, but not divergent squint; (2) no evidence of true squint on initial examination; (3) a follow-up of either (i) one year—71 cases; or (ii) to a time when a final orthoptic report including the visual acuity of each eye could be completed—260 cases.

Refractive errors are an important aspect of convergent squints and were tested after giving atropine ointment. In this study a refractive error is defined as one of +1·50 D or more in any meridian of the more ametropic eye. Contrariwise, emmetropia is +1·50 D or less in any meridian in the more ametropic eye. The overlap is deliberate to emphasise the arbitrariness of the level of error chosen. 0·50 D was deducted from the retinoscopy in respect of the cycloplegia and 1·00 D or more if appropriate for the working distance—i.e., 1·50 D—a working distance of 1 metre being

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Table 1 *Pseudostrabismus: incidence of*

Squint *23/331*	*Ametropia* *77/320*	*Squint + ametropia* *19/320*
6·9%	24%	5·94%

Table 2 *Pseudostrabismus: incidence of squints*

In ametropes *19/77*	*In emmetropes* *4/243*
24%	1·65%

assumed. With small children the working distance would be less. Various figures for the incidence of refractive errors have been reported, but authors are not always careful to define what they mean by the term. Refractive errors suggest a piece of string if not a piece of elastic—how much or how long?—and our figure which takes into account errors likely to be pertinent to convergent squint is a good criterion for the comparative purposes of this study. There were only 2 children with myopia in the whole group.

Results

The age at which the children were first seen varied from 2 months to 5 years. A family history was deemed to be positive if any relative, however distant, was said to be affected by a squint. Of 284 cases in which information was available 113 (39·8%) had a positive family history. Of 54 patients with refractive errors 30 (55·6%) had a positive family history. Of 230 without refractive errors 83 (36·1%) and of those 17 cases in whom a squint was subsequently confirmed 12 (70·6%) had a positive family history. Suggestive though they may be, the figures are insufficient to be statistically significant. There are too many positives to make the family history helpful in cases of pseudostrabismus.

Of the 321 cases only 23 were found to have a convergent squint or phoria on follow-up. These figures are illustrated by Table 1. However, the really interesting figures are presented in Table 2. Of emmetropes with pseudostrabismus only 4 of 243, that is 1.65% subsequently developed squint—a figure much less than the average incidence in a non-selected group of children.

Discussion

The above findings indicate that we can manage patients referred as convergent squints and who on initial examination are thought to have pseudostrabismus (that is over 60% of them) as follows: (1) Refract them; (2) discharge the emmetropes; (3) follow-up the ametropes. Thus we can save 243/320, that is, 76% of patient visits, and a colossal amount of parent time.

The more cautious ophthalmic surgeons may suggest to the parents that they bring their emmetropic child for a vision test at the age of 4 years.

I am grateful to my orthoptist, Mrs A. Richards, and my secretary, Mrs V. Mumford, for their help in the retrieval, and to Dr A. S. Harris, of the West Sussex Area Health Authority, who provided some of the figures from the National Child Development Study (1958 cohort).

References

Graham, P. A. (1974). Epidemiology of strabismus. *British Journal of Ophthalmology*, **58**, 224–231.

Pratt-Johnson, J. A., and Lunn, C. T. (1967). Early case finding and the hereditary factor in strabismus. *Canadian Journal of Ophthalmology*, **2**, 50–53.

Worth, C., and Chavasse, B. (1959). Squint: the binocular reflexes and the treatment of strabismus, 9th edn., p. 375. By T. Keith-Lyle and G. J. O. Bridgeman. Baillière, Tindall and Cox: London.

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The O'Connor cinch revisited

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SUMMARY The modified O'Connor cinch operation is a useful, but little used, adjustable resection operation. For increased understanding of its shortening and adjustment characteristics, a standard cinch was performed in animals and patients with strabismus. Animal studies showed that, as each strand of the cinch was removed, a small, relatively equal release of the cinch effect occurred. Measurement of the shortening obtained in patients with strabismus showed a consistent resection effect of about 4 mm.

Review of 17 cases in which the cinch was used as part of the surgical treatment showed the technique to be adjustable by reducing the overcorrection in 6 cases. Ten to 20 prism dioptres of reduction in the deviation was obtained with adjustment of the cinch on the first postoperative day. All 17 cases had satisfactory adjustment. The largest residual deviation was 12 prism dioptres.

O'Connor (1916) described a new operation for shortening a muscle with an effect analogous to that of a resection. The technique involved splitting the tendon into 2 lateral strips and a central tongue, and then shortening the lateral strips with loops of catgut before securing the central tendon to the sclera anterior to the insertion. McCool (1930) reviewed the procedure and quantified the shortening effect of the cinch in 32 operative cases and 6 pathological specimens. He concluded that the shortening was predictable and the effect was dependent on the width of the tendon strips, the number of strips, and the calibre of the suture strands. Durr (1937) pointed out the popularity of the cinch operation in San Francisco but its limited use elsewshere in the country. He suggested the reason for the limited use of the cinch was related to a poor understanding of the fine points of technique upon which the success of the operation depends.

Today the cinch operation has all but fallen into oblivion. It has recently been revived by Jampolsky (1975) in a modified form, as a method of adjustable resection. The indications, methods, effect, and understanding of how the cinch works are not generally known, so this useful strabismus operation suffers the same obscurity now as 35 years ago.

Adjustable suture techniques have proved a very useful tool of the strabismus surgeon (Rosenbaum *et al.*, 1977). The O'Connor cinch is a safe and effective adjustable resection technique and can be used in both adults and children.

The purpose of this paper is (1) to quantitate the amount of muscle shortening achieved with a standard cinch; (2) to examine the way in which the muscle lengthens as the cinch is released; and (3) to review the results in a series of patients in which the cinch was used.

Methods

TECHNIQUE OF MODIFIED CINCH

The cinch technique used in the study was performed in the following way.

(1) The muscle and its tendon were exposed through a conjunctival incision over the muscle insertion. The tendon was identified, freed of intramuscular membrane, and lifted on a muscle hook. A curved tendon-splitter (small, sharpened muscle hook—Fig. 1) was used to split the muscle in half, extending 5 to 6 mm back from the insertion. Each half of the muscle was then split again, producing 4 equal slips of muscle and tendon.

(2) A cinch cable was made from 4 strands of 3–0 nylon threaded through a large, curved, blunted needle (Fig. 2). The ends of the suture were tied in a knot or melted together with a cautery to make an 8-strand cable.

(3) After the end of the cable was clipped to the drape near the eye it was looped round the first muscle slip. As the cable was threaded under the muscle slip it was directed toward the cornea. The cable was then looped round each of the remaining slips, being directed away from the cornea on the second loop, towards the cornea on the third loop, and away from the cornea on the forth loop (Fig. 3*a*).

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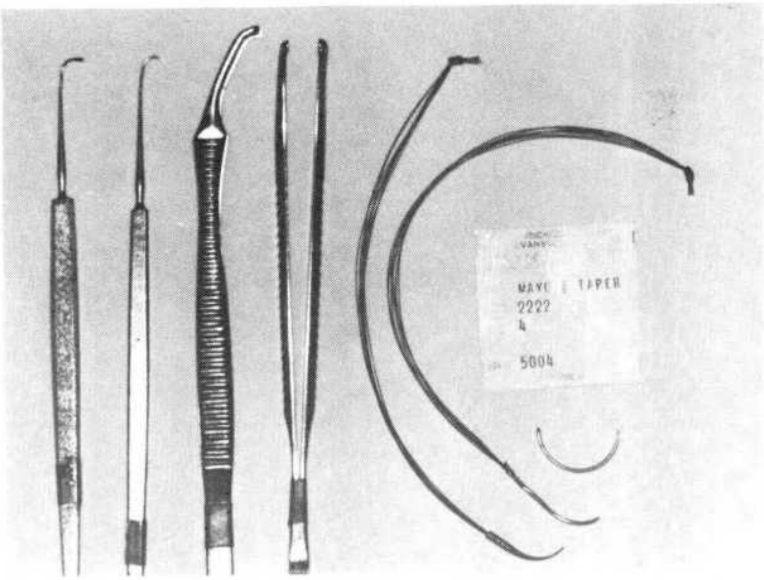

Fig. 1 *Instruments needed for the cinch procedure. From left to right there is a small, rounded muscle hook, a small, sharp-tipped muscle hook (useful for muscle splitting), side view of a forceps to fixate the cinch cable when tightening the cable, a top view of the same forceps, and 2 cinch cables attached to blunt-tipped needles*

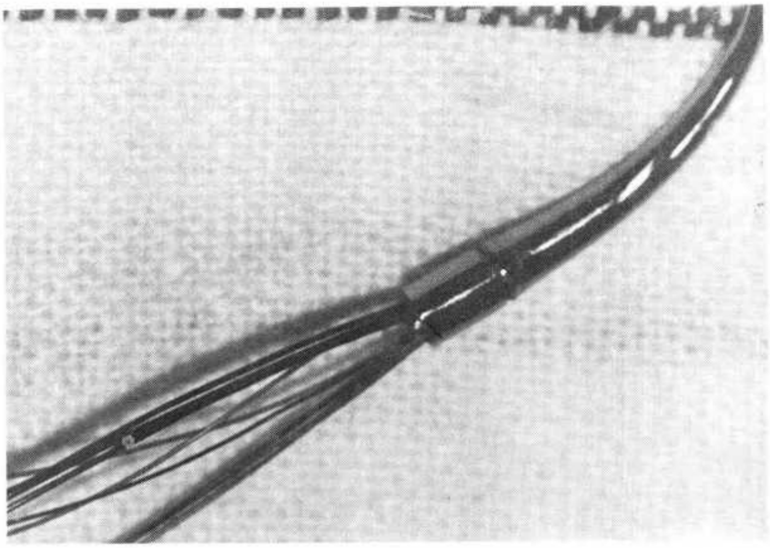

Fig. 2 *Close-up view of the blunt-tipped needle with the attached strands of nylon cable for performing the cinch operation*

Alternating the direction of the loops produces a more effective cinch on the muscle, and the long end of the cable that exits through the conjunctiva will be directed away from the cornea. The cinch was then pulled tight (Figs. 3*b, c, d*), forceps (Fig. 1) being used to hold the suture cable at one edge of the muscle. As the cinch was pulled taut, first on one margin of the muscle and then on the other, it effectively shortened the muscle (Fig. 3*d*). The nylon cable was then cut 1 or 2 mm from the superior margin of the muscle while the inferior end was brought out through the conjunctiva to rest in the lower cul-de-sac. This end of the cable was left long enough to rest horizontally inside the lower lid. The conjunctiva was closed with interrupted sutures, with particular attention to form a tight closure about the nylon cable.

Patients were examined within 24 hours of surgery to determine the adequacy of alignment and the need for adjustment of the cinch. If a cover test in the sitting position showed a significant overcorrection, adjustment was performed. To make the

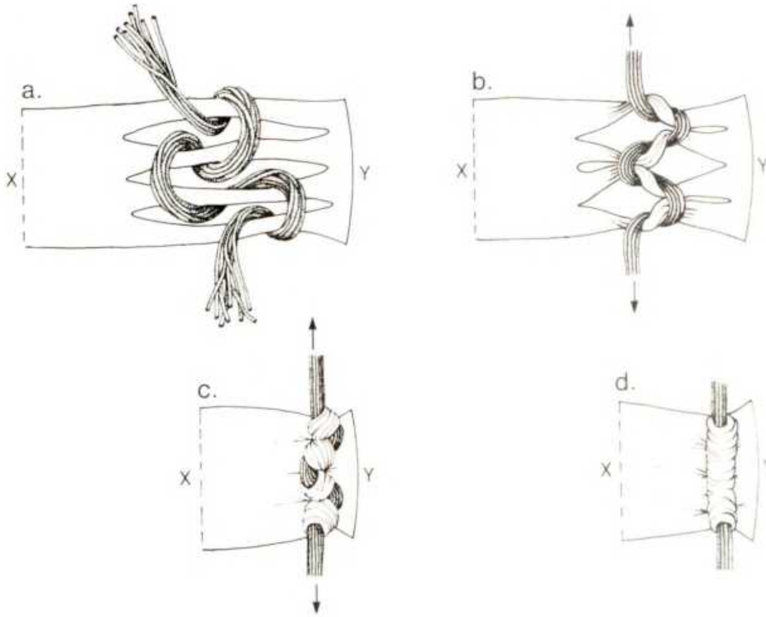

Fig. 3 *Diagram of the cinch procedure.* (*a*) *The muscle has been split into 4 strands. The cinch cable has been woven around each of the strands.* Y *marks the muscle insertion,* X *marks a point on the muscle posterior to the area of muscle that has been split.* (*b*) *The cable is being tightened, causing the muscle to begin shortening.* (*c*) *Further tightening of the cable.* (*d*) *The cable is fully tightened, cinching and thus shortening the muscle (shorter distance between a fixed point on the muscle posteriorly* (X) *and the insertion* (Y))

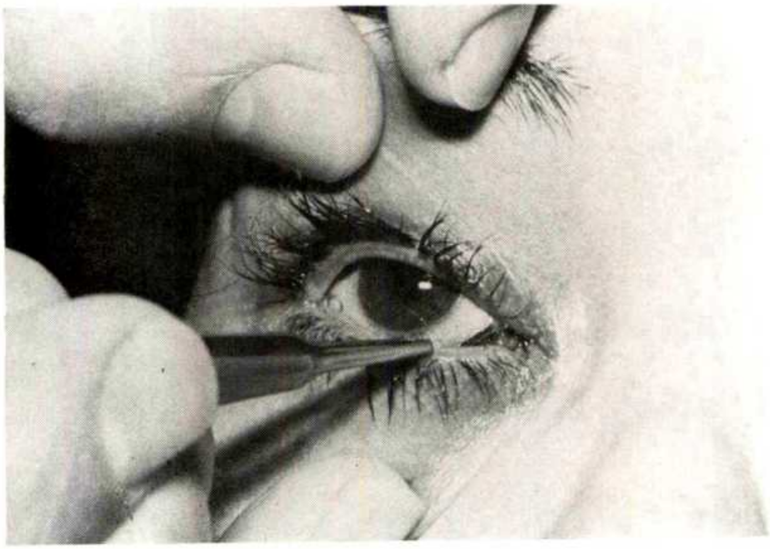

Fig. 4 *Removal of a strand of the cinch cable. The lids are held apart. After a drop of topical anaesthetic has been instilled, a forceps is used to grasp 1 of the strands, and the strand is removed by sliding it out horizontally. The cinch cable can be seen as several black strands adjacent to the caruncle*

adjustment, the lower lid was everted and the cable exposed. With forceps a single strand of the cable was removed by gently sliding it out in a horizontal direction (Fig. 4). The patient was then asked to make horizontal saccades for a minute or two and the cover test was repeated. Additional strands of cable were removed, one at a time, until the alignment was satisfactory or all the strands were removed.

If no adjustment was required, the cable was not removed until 14 days postoperatively. At that time the entire cable was removed 1 strand at a time.

QUANTITATIVE STUDIES

To study the shortening and unwinding characteristics of the cinch, separate clinical and laboratory studies were done.

Animal experiments. Nine dogs were anaesthetised and an 8-strand, 3–0 nylon cinch looped once around 4 strips of each lateral rectus muscle. The amount of shortening was measured utilising a marking suture placed in the body of the muscle and measuring its change in position relative to the muscle insertion following the cinch procedure. One day later the conjunctiva was re-opened and the cinch undone 1 strand at a time. The change in length of the muscle per strand removed was measured in the same way.

Clinical measurements. Five patients undergoing strabismus surgery had a cinch of 1 muscle performed in a standard manner using 8 strands of 3–0 nylon looped once around 4 muscle strips. The shortening obtained was measured by the change in position of a silk suture placed in the body of the muscle relative to the insertion.

CLINICAL SERIES

Since 1974 17 patients with strabismus had a cinch procedure as part of their surgical treatment. These cases were evaluated with particular attention to the following criteria: (1) length of follow-up, (2) amount of correction obtained with adjustment, (3) stability in the postoperative period, and (4) final postoperative result. The patients ranged in age from 2¼ to 57 years. All the cinches were performed on a horizontal rectus muscle, and the antagonist muscle was weakened with a recession or a 'Z' tenotomy. With the exception of 2 minimally scarred muscles all the cinches were performed on previously unoperated muscles.

Results

QUANTITATIVE STUDIES

Animal experiments. The amount of shortening of the lateral rectus muscle obtained with a standard cinch in 9 dogs of different breeds varied from 2 to 7 mm. The shortening for each lateral rectus pair was similar. Removal of the cable, 1 strand at a time, resulted in muscle lengthening in small, relatively equal increments. The muscle lengthening was approximately linear, ranging between 0·25 and 0·5 mm increase in muscle length per strand removed.

Operative measurements. Five patients had measurements of the amount of shortening obtained with our standard cinch. The cinch procedure shortened the muscle an average of 4 mm, with a range of 3 to 5 mm.

CLINICAL SERIES

In 17 patients a cinch was used as part of the surgical procedure. Follow-up ranged from 1 to 6 months with an average of 3·5 months. Eighteen cinches were used in these 17 patients. Of these, 6 were adjusted.

The preoperative deviations averaged 28 prism dioptres (range 80 prism dioptres of exotropia to 40 prism dioptres of esotropia).

Adjustment was done within 24 hours in 4 patients and 6 days postoperatively in 2 patients. Preadjustment deviations, as determined by cover test, ranged from 12 to 25 prism dioptres. Of those patients adjusted on the first postoperative day there was an immediate reduction in the deviation of 10 to 20 prism dioptres; those adjusted on the sixth day had a reduction of 3 to 10 prism dioptres. Three of the 4 cases adjusted on the first postoperative day had an additional 8 to 15 prism dioptre spontaneous reduction of the deviation in the following 2 to 4 weeks. The average change was 12 prism dioptres. The fourth case and the 2 patients adjusted on the sixth postoperative day showed no drift after adjustment. Of the 6 cinches adjusted 4 had no residual deviation, 1 had 8 prism dioptres of esotropia, and the other had 10 dioptres of exotropia.

The final residual deviation in this series of 17 patients varied from 10 dioptres of exotropia to 12 dioptres of esophoria. Eight patients had less than 2 dioptres of residual deviation, 5 had between 2 and 5 dioptres of esotropia, 1 had 12 dioptres of esophoria, and 3 had between 2 and 10 dioptres of exotropia. The average residual deviation was approximately 2 prism dioptres. None of these patients required additional surgery.

Discussion

Data from our studies illustrate several important characteristics of the cinch procedure. With a standard procedure a predictable muscle shortening occurs in man. This averaged 4 mm of resection. This amount of resection is frequently the maximum effect desired in vertical rectus surgery and can be sufficient when operating on tight horizontal rectus muscles or when 3 or 4 horizontal rectus muscles are operated upon at the same time.

It also gives consistent shortening in lateral rectus muscle pairs in animals. The wide difference in effective muscle shortening by the cinch between animals is probably due to the varying width of the lateral rectus muscles among dogs of different size and breed. The release of the cinch occurs in a graded fashion in animal studies. As each cable is removed, there is a relatively equal, incremental release of the cinch effect.

Clinical data show that there is an additional 'stretching out' of the cinch effect for 2 to 4 weeks after adjustment. A 10 to 20 dioptre reduction in the deviation can be achieved with removal of some or all of the cinch strands on the first postoperative day. When the entire cinch is removed, the muscle unwinds completely, thus minimising the effect of recession of the antagonist. The cinch can be adjusted only in one direction; it can be loosened or removed, not tightened.

The cinch can be used in children over the age of 3. If adjustment is required in a child, one instills a topical anaesthetic, pulls down the lower lid, picks up 1 strand of the cable with forceps, and gently slides it out horizontally. There is minimal discomfort to the patient, not unlike removing skin sutures.

Although the average follow-up is relatively short (3·5 months), the mechanical effect of any strabismus procedure is set approximately 8 weeks after surgery. Changes in the deviation after 3·5 months would not be the result of the type of surgery used, as no operative technique promises excellent results for an unlimited time.

We have encountered no complications resulting from this procedure. Patients may experience some minor discomfort from the cable resting in the cul-de-sac along with mild conjunctival hyperaemia. Occasionally the cable may pop out from beneath the lower lid, but it is easily replaced. There have been no postoperative infections as a result of the cinch.

The cinch procedure may be used in cases where the option for postoperative adjustment is desired. This might include patients with fusion capability, cases in which the surgical effect is somewhat unpredictable, or patients too young to co-operate for the 'standard' adjustable technique (ages 3 to 14). It is not recommended for use on previously operated muscles, as the effect of the cinch may be difficult to predict because of scarring. It should be reserved for children over the age of 3, as some patient co-operation is required.

The advantages of the cinch operation are: (1) it is a safe operation, as no scleral sutures are required; (2) it is easily performed; (3) it is an adjustable resection technique; (4) it can be used in adults and children; (5) it is reversible by removing the cinch cable on the first postoperative day.

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References

Durr, S. A. (1937). The O'Connor cinch-operation technique. *American Journal of Ophthalmology*, **20**, 178–180.

Jampolsky, A. (1975). Strabismus reoperation techniques. *Transactions of the American Academy of Ophthalmology and Otolaryngology*, **79**, 704–717.

McCool, J. L. (1930). Some original experiments with the O'Connor muscle-shortening operation. *American Journal of Ophthalmology*, **13**, 491–495.

O'Connor, R. (1916). A new shortening technique with report of forty-two operations. *Journal of the American Medical Association*, **67**, 268–276.

Rosenbaum, A. L., Metz, H. S., Carlson, S., and Jampolsky, A. (1977). Adjustable rectus muscle recession surgery. *Archives of Ophthalmology*, **95**, 817–823.

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Bilateral versus unilateral cataract extraction: advantages and complications

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SUMMARY Cataract extraction was performed on 734 patients. These were followed up postoperatively for up to 1 year. In 448 cases the extraction was performed in both eyes during 1 operating session (896 eyes) and in 1 eye in 286 cases, a total of 1182 cataract extractions. Preoperatively more than 75% of the eyes in both groups had perception of light only. Postoperatively more than 85% of eyes in both groups achieved a visual acuity of 6/30 or better. The postoperative visual performance of an eye was not influenced by the mode of operation, bilateral or unilateral.

The overall incidence of complications among the 1182 operated eyes was: accidental extracapsular cataract extraction 10·2%, vitreous loss 11·0%, hyphaema 1·4%, flat anterior chamber 0·9%, dehiscence of the wound 0·5%, uveitis 1·2%, endophthalmitis 0·3%, secondary glaucoma 0·9%, severe bullous keratopathy 1·4%, oedema of the macula 0·5%, and retinal detachment 0·3%. The complications in both groups of patients were comparable. Only in 1 case operated in both eyes vision was not restored following a bilateral endophthalmitis.

Though the advantages of performing a bilateral cataract extraction on a suitable patient during 1 operating session in a developed country are obvious (Duthie, 1955; Manschot, 1959), it is not performed routinely (Deller, 1976). In a developing country economic factors such as the shortening of the period of hospitalisation, the possibility of using only 1 suture and the same instruments for operating both eyes, and the need to dispense only 1 pair of glasses postoperatively are other advantages which must be considered. Also, the possibility that a patient operated upon in only 1 eye will disappear and not seek the operation for the other eye adds another factor favouring bilateral extraction. The main disadvantages and drawbacks to this approach have been the fear of a bilateral complication leading to blindness in both eyes.

During a period of 16 months we operated 1549 cataracts. We were able to follow-up 448 cases of bilateral extractions (896 eyes) and 286 cases of unilateral extractions (286 eyes) for a period of up to 1 year. This is a report comparing the visual results and the complications in both groups of patients.

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Materials and methods

Males and females with opacities of the lens were admitted for operation. The assignment for bilateral or unilateral cataract extraction was made according to the visual acuity. Patients with a visual acuity of 6/60 or less in the better eye were usually assigned to a bilateral cataract extraction. Unilateral cataract extraction was performed in cases where a visual acuity better than 6/60 was recorded in 1 eye. Four cases with a visual acuity between 6/60 and 6/12 in the better eye were operated bilaterally because of secondary considerations. Patients referred from peripheral dispensaries and district hospitals were examined under the slit lamp, and the intraocular pressure was recorded with an applanation tonometer (BenEzra and Chirambo, 1978*a*). Preoperative assessment of retinal function was evaluated by the ability to percept a dim source of light in all directions of visual field.

SURGICAL PROCEDURE

General or local anaesthesia was used randomly throughout the period of study. The surgery was performed as described previously (BenEzra and Chirambo, 1978b). Briefly, a fornix-based conjunctival flap was secured and a corneal incision of 150° to 170° made at the limbus. Peripheral or sector iridectomy was performed according to the lens status. Lens extraction was carried out with forceps or erisiphake by tumbling or sliding. No chymotrypsin was used for zonulysis. In cases of accidental rupture of the capsule, lens remnants were gently washed out with saline. The surgical wound was closed with three 7–0 or six 8–0 sutures (1 of which is a preplaced suture in each case). In cases of vitreous loss conservative anterior vitrectomy was performed and the wound carefully cleaned. Postoperative treatment, follow-up, and classification of visual acuity achieved were performed as previously described (BenEzra and Chirambo, 1978b).

Results

Cataract extraction was undertaken in 1549 eyes, 1182 were available for follow-up. In 448 cases the operation was on both eyes (896 eyes) and in 286 cases on 1 eye. We believe that the loss for follow-up was at random, so that the cases available represent adequately all the eyes operated upon.

Among the eyes operated upon in bilateral operations only 0·5% had a preoperative visual acuity better than 6/60. After operation 89·4% achieved a visual acuity better than 6/60 (Table 1). The eyes in cases undergoing unilateral extraction had in general a worse preoperative visual acuity. Only 2·8% showed a visual acuity of 3/60 to 6/60 and none had a visual acuity better than 6/60. After operation 87·8% achieved a visual acuity better than 6/60 (Table 2).

Table 3 illustrates the complications encountered during the bilateral cataract extractions. The commonest was vitreous loss in 10·7% of the eyes. Vitreous was lost in both eyes in 23 cases (5·1%), that is, 47·7% of the vitreous losses in this group occurred in both eyes. An accidental extracapsular cataract extraction occurred in 9·9% of the eyes; 3·6% were bilateral. However, vitreous loss and extracapsular cataract extraction occurred bilaterally only in 2 cases. Hyphaema persisting for more than 72 hours after operation was observed in 1·6% of cases; in 0·7% it occurred in both eyes. Uveitis was observed in 1·2% of the cases and only in 1 case bilaterally (0·2%). Endophthalmitis occurred in 3 eyes (0·3%), 1 bilateral case (Table 3). Other complications such as flat anterior chamber persisting for more than 48 hours, dehiscence of the wound, secondary glaucoma, severe bullous keratopathy, oedema of the macula, or retinal detachment occurred in 0·2 to 1·3% of the operated eyes in this group. None of these occurred in both eyes of the same patient (Table 3).

Table 1 *Pre- and postoperative visual performance among the 448 cases operated bilaterally (896 eyes)*

	Before operation *No.*	*%*	*After operation* *No.*	*%*
LP–HM	691	77·1	25	2·8
1/60–2/60	148	16·5	22	2·5
3/60–6/60	53	5·9	48	5·4
6/30–6/12	4	0·5	606	67·6
6/9–6/6	0	0	195	21·8
Total	896	100	896	100·1

Table 2 *Pre- and postoperative visual performance among 286 cases operated unilaterally*

	Before operation *No.*	*%*	*After operation* *No.*	*%*
LP–HM	225	78·7	5	1·7
1/60–2/60	53	18·5	16	5·6
3/60–6/60	8	2·8	14	4·9
6/30–6/12	0	0	189	66·1
6/9–6/6	0	0	62	21·7
Total	286	100·0	286	100·0

Table 3 *Complications after bilateral cataract extraction*

Complication	*Right eyes* *No.*	*%*	*Left eyes* *No.*	*%*	*Both eyes* *No.*	*%*	*Total eyes* *No.*	*%*
ECCE*	27	3·0	30	3·3	16	3·6	89	9·9
Vitreous loss	23	2·6	27	3·0	23	5·1	96	10·7
Hyphaema	6	0·7	2	0·2	3	0·7	14	1·6
Flat AC†	4	0·4	3	0·3	—	—	7	0·7
Dehiscence of wound	2	0·2	3	0·3	—	—	5	0·6
Uveitis	5	0·6	4	0·4	1	0·2	11	1·2
Endophthalmitis	—	—	1	0·1	1	0·2	3	0·3
Secondary glaucoma	6	0·7	1	0·1	—	—	7	0·8
Bullous keratopathy	5	0·6	6	0·7	—	—	12	1·3
Oedema of macula‡	2	0·2	2	0·2	—	—	4	0·4
Retinal detachment	1	0·1	1	0·1	—	—	2	0·2

* ECCE = Extracapsular cataract extraction (accidental). † AC = Anterior chamber. ‡ Recorded when obvious oedema was observed ophthalmoscopically and vision was markedly impaired

Among the cases operated upon unilaterally accidental extracapsular cataract extraction occurred in 11·0% of the cases and vitreous loss in 11·9%. These seemed to occur at a higher frequency in left than in right eyes (Table 4). All other complications were observed in an incidence ranging from

Table 4 *Complications after unilateral cataract extraction*

Complication	*Right eyes* *No.*	*%*	*Left eyes* *No.*	*%*	*Total eyes* *No.*	*%*
ECCE*	14	4·8	18	6·2	32	11·0
Vitreous loss	13	4·5	21	7·3	34	11·9
Hyphaema	—	—	3	1·0	3	1·0
Flat AC†	2	0·7	2	0·7	4	1·4
Dehiscence of wound	1	0·3	—	—	1	0·3
Uveitis	1	0·3	2	0·7	3	1·0
Endophthalmitis	1	0·3	—	—	1	0·3
Secondary glaucoma	2	0·7	2	0·7	4	1·4
Bullous keratopathy	3	1·0	1	0·3	4	1·4
Oedema of macula‡	1	0·3	1	0·3	2	0·7
Retinal detachment	—	—	1	0·3	1	0·3

* ECCE = Extracapsular cataract extraction (accidental). † AC = Anterior chamber. ‡ Recorded when obvious oedema was observed ophthalmoscopically and vision was markedly impaired

0·3 to 1·4% similarly to the group operated bilaterally.

Discussion

The postoperative visual performance among the cases operated upon bilaterally and those operated upon unilaterally was strikingly similar. Among the cases operated on bilaterally 89·4% achieved a visual acuity of 6/30 or better (21·8% achieved a visual acuity of 6/9 or better). Among the cases operated on unilaterally 87·8% achieved a visual acuity of 6/30 or better (21·7% showed a visual acuity of 6/9 or better). The relatively low incidence of eyes achieving a very good postoperative vision in both groups was due to the approximative refractive correction and the frequent senile macular changes. However, owing to the specific conditions of living, a visual acuity of 6/30 was considered reasonable because it enabled these patients to live a normal life in their community. The percentage of eyes with a poor or very poor visual acuity after operation was also similar in both groups.

There was a nearly similar incidence of accidental extracapsular cataract extraction among both groups of patients. Most of these were due to intumescent lenses. Vitreous loss has been considered as a major complication during cataract surgery (Jaffee, 1972) and a serious threat for postoperative vision (Dunphy, 1927; Vail, 1965). In a previous study (BenEzra and Chirambo, 1978b) it was shown that although vitreous loss during cataract extraction may comprise the chances of an eye to have very good postoperative vision, it was not a disaster. The relatively good vision achieved by the eyes with vitreous loss might be attributed to better treatment and/or to the fact that in most cases the vitreous was fluid and easy to manage (BenEzra and Chirambo, 1978b). These results are in line with those reported by Krasner (1973) on a small number of patients.

Hyphaema persisting for more than 72 hours after the operation, flat anterior chamber persisting for more than 48 hours, or dehiscence of the wound were observed in few cases, and their incidence was similar in both groups of patients. These complications were treated successfully by conservative measures in most cases. In 3 cases of dehiscence of the wound iridectomy and resuturing were performed under general anaesthesia. Secondary glaucoma with an intraocular pressure ranging from 28 to 55 mmHg occurred in 0·8% of the eyes after a bilateral extraction procedure. None of these had secondary glaucoma in both eyes. Among the group operated upon in 1 eye the incidence of secondary glaucoma was 1·4%. All eyes with secondary glaucoma were initially treated medically with a poor response. Surgery was performed at a later stage in all those eyes.

The most serious complication encountered was the postoperative endophthalmitis. Prophylactic antibiotic treatment before surgery has very little effect (Chalkley and Shoch, 1967) or no influence (Allen and Mangiaracine, 1973) on the incidence of postoperative endophthalmitis. More recently a drastic lowering of bacterial endophthalmitis from an incidence of 3·6 to 0·37% after cataract extraction in the eye camps of South India has been achieved by the prophylactic intracameral injection of 50 μg gentamicin (Peyman *et al.*, 1977). It should be stressed, however, that the comparisons in the latter study have been made between heterogeneous groups operated on by different surgeons. Therefore, although possibly real, the seeming effectiveness of intracameral gentamicin in abolishing 99% of the endophthalmitis in these camps should be more carefully analysed. In our series no prophylactic antibiotics were used, and an overall incidence of 0·3% has been encountered. Two eyes were affected in 1 case. The bilateral endophthalmitis in this case was observed along with a general bacteraemia and dysentery developing 24 hours after the operation. Intensive therapy with intravenous penicillin and oral chloramphenicol improved the general condition of the patient within 10 days. However, the ocular condition did not improve, and both eyes remained with a perception of hand movements only. The other 2 eyes with endophthalmitis (1 eye in the bilateral group and the only eye affected in the unilateral group) did not respond to systemic and topical treatment with antibiotics. No useful vision was retained in the affected eyes. The visual acuity in the fellow eye of the bilateral case was 6/9. Late aseptic endophthalmitis, although reported by others (Gleicher and Welch, 1973), was not observed in our series during the 1-year follow-up.

Postaphakic retinal detachment was observed in 2 eyes (0·2%) in different patients operated on bilaterally, and in 1 eye of the unilateral group (0·3%). This incidence is much lower than the incidence observed in Caucasians (Roussos and Polychroniadis, 1973). The low frequency of spontaneous or primary retinal detachment as observed in this study may be due to congenital factors. It is tempting to postulate that the lower frequency of primary retinal detachment (AvShalom *et al.*, 1967a, b) and the very low incidence of postaphakic retinal detachment in Africans is connected with the higher fundal pigmentation and a tighter adhesion between pigment epithelium and neuroretina. A very low incidence of primary retinal detachment was also observed among blacks in the United States (Brown and Thomas, 1965). These investigators also reported a lack of postaphakic retinal detachment among their black patients, whereas 44% of the white patients with retinal detachment were aphakic.

Severe uveitis in 1·2 and 1% of the bilateral and unilateral groups respectively was observed in all cases on the second or third month after operation. Most of these eyes responded well to combined treatment with topical antibiotics and topical or systemic steroids.

Severe bullous keratopathy was observed in few cases; all resulted in a very poor visual performance. This complication was closely correlated with vitreous loss and accidental extracapsular cataract extraction occurring in the same eye. However, bullous keratopathy was not observed in both eyes of the same patient, although vitreous loss and extracapsular cataract extraction occurred bilaterally in 2 cases.

These data clearly indicate that the complications encountered during a bilateral cataract extraction are comparable to those observed when 1 eye is operated. Only in 1 unfortunate case was vision lost in both eyes due to endophthalmitis. The possibility of a complication occurring during a 'delayed' operation of 1 of the eyes in this case cannot be ruled out. However, it is undeniable that if the operation had been deferred in 1 of the eyes, the chances are that vision could have been kept in 1 eye. Such an argument is of colossal psychological influence on the surgeon's decision, and the obvious advantages of the bilateral approach in controlled conditions and adequate patients should be strongly considered against it.

In a developing country the socioeconomic factors are so important that the slender possibility of a complication in both eyes is a calculated risk which should not interfere with the routine performance of a bilateral cataract extraction during one operating session.

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References

Allen, H. F., and Mangiaracine, A. B. (1973). Bacterial endophthalmitis after cataract extraction: II. Incidence in 36 000 consecutive operations with special references to preoperative topical antibiotics. *Transactions of the American Academy of Ophthalmology and Otolaryngology*, **77**, 581–588.

AvShalom, A., Berson, D., Gombos, G. M., Michaelson, I. C., and Zauberman, H. (1967a). Some comments on the incidence of idiopathic retinal detachment among Africans. *American Journal of Ophthalmology*, **64**, 384–386.

AvShalom, A., Berson, D., Gombos, G. M., Landau, L., Michaelson, I. C., and Zauberman, H. (1967b). The vitreoretinopathy associated with retinal detachment among Africans. *American Journal of Ophthalmology*, **64**, 387–391.

BenEzra, D., and Chirambo, M. C. (1978a). Trabeculectomy. *Annals of Ophthalmology*, **10**, 1101–1105.

BenEzra, D., and Chirambo, M. C. (1978b). Vitreous loss during intracapsular cataract extraction. *Annals of Ophthalmology*. (In press.)

Brown, P. R., and Thomas, R. T. (1965). The low incidence of primary retinal detachment in the Negro. *American Journal of Ophthalmology*, **60**, 109–110.

Chalkley, T. H. F., and Shoch, D. (1967). An evaluation of prophylactic subconjunctival antibiotic injection in cataract surgery. *American Journal of Ophthalmology*, **64**, 1084–1087.

Deller, M. (1976). Operation simultanée des cataractes bilaterales. *Ophthalmologica*, **172**, 143–148.

Dunphy, E. B. (1927). Loss of vitreous in cataract extraction. *Journal of the American Medical Association*, **89**, 2254–2257.

Duthie, O. M. (1955). Bilateral cataract extraction. *Transactions of the Ophthalmological Societies of the United Kingdom*, **75**, 25–31.

Gleicher, D. A., and Welch, R. B. (1973). Late aseptic endophthalmitis after cataract surgery. *American Journal of Ophthalmology*, **75**, 769–773.

Jaffee, N. S. (1972). *Cataract Surgery and its Complications*, 1st edn., p. 124. Mosby: St. Louis.

Krasner, D. (1973). Vitreous loss during cataract surgery. *Transactions of the American Academy of Ophthalmology and Otolaryngology*, **77**, 184–185.

Manschot, W. A. (1959). Bilateral cataract extraction. *Ophthalmologica*, **137**, 428–430.

Peyman, G. A., Sathar, L. M., and May, D. R. (1977). Intraocular gentamicin as intraoperative prophylaxis in South India eye camps. *British Journal of Ophthalmology*, **61**, 260–262.

Roussos, J., and Polychroniadis, F. (1973). Le decollement de la retine, suite a l'extraction de la cataracte. *Annales d'Oculistiques*, **206**, 315–319.

Vail, D. (1965). After-results of vitreous loss. *American Journal of Ophthalmology*, **59**, 573–586.

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Follow-up of aphakic patients with anterior vitrectomy in one eye and uneventful cataract extraction in the fellow eye

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SUMMARY Twenty patients had operations for bilateral cataract in 2 separate sessions, with uncomplicated extraction on one side and vitreous loss managed with anterior vitrectomy on the other. The cataracts, the type of surgery, and the postoperative treatment were identical in both eyes.

The differences between the 2 eyes were not statistically significant so far as the amount of astigmatism, final visual acuity, and peripheral anterior synechiae were concerned. The main difference was found to be the period of time the vitrectomised eyes remained red and uncomfortable as compared to the eyes with uncomplicated surgery.

Since cataract extraction replaced couching over 200 years ago vitreous loss has been the most dreaded complication—after expulsive haemorrhage—occurring during cataract surgery. The sequelae of this complication are not related to the amount of vitreous lost during the operation, and they can occur in cases in which only the anterior hyaloid membrane is ruptured without manifest outpouring of vitreous through the wound. These complications are due to 4 mechanisms (Jaffe, 1972): Direct contact of vitreous with other structures (cornea, filtration angle, etc.); incarceration of vitreous in the surgical wound; inflammation; and fibrosis of the residual vitreous.

In an effort to overcome the first 2 of these mechanisms (and consequently reduce the risk of the last 2) Maumenee (1957) described the technique of aspirating fluid vitreous through the pupil and sweeping away all vitreous strands from the wound. Kasner (1968) suggested the use of scissors to cut formed vitreous as it adheres to Weck cell sponges introduced through the pupil, while Gass (1970) recommended the combination of these 2 techniques.

Whichever method is employed, surgeons throughout the world perform anterior vitrectomy today in an attempt to minimise the postoperative complications of vitreous loss. Indeed, since anterior vitrectomy has been used encouraging reports have appeared in the literature on the outcome of the eyes (Cerasoli and Kasner, 1971; Mazjna Miyake, 1972; Uchino, 1975; Luntz, 1977).

This study reports on the results of anterior vitrectomy performed on 1 eye of patients with bilateral surgery for cataracts who had an uneventful extraction in their fellow eye. This provided an objective comparison on the outcome of the 2 eyes of the same patient.

Material and methods

All patients with bilateral mature cataracts have their cataracts removed at an interval of 2 to 14 days between the 2 eyes. To ensure as much similarity as possible between the 2 eyes the patients had to meet the following requirements in order to qualify for this study: No other pre-existing unilateral eye disease; identical surgical approach to both eyes (i.e., corneal section or limbal section).

Patients with surgical complications such as capsule rupture were excluded from the study. The only exception were those patients who had vitreous loss and anterior vitrectomy in the first eye. In these cases surgery for the second eye was performed by a consultant and under general anaesthesia whenever possible.

Local anaesthesia was the rule. The incision was either limbal (under a conjunctival flap) with 9–0 virgin silk sutures, or a corneal section with 10–0 nylon monofilament sutures. An operating micro-

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scope was used in all cases. Chymotrypsin was used in patients under the age of 55 and the lens was delivered with the cryoextractor.

Whenever rupture of the anterior hyaloid membrane was encountered (with or without manifest bulk-loss of vitreous), anterior vitrectomy was performed by the technique described by Gass (1970).

Postoperative treatment was identical in both eyes—atropine and a steroid-antibiotic combination, both given as drops twice and four times daily for 4 to 6 weeks after surgery.

All patients were discharged from the hospital 7 to 10 days after the operation on the second eye and seen again 2, 4, 8, and 12 weeks after discharge. Thereafter follow-up was at 3-monthly intervals. On each visit the general appearance of the eyes was noted, corrected visual acuity was checked, keratometry was performed, and intraocular pressure measured, anterior chamber activity and pupil state were assessed, and finally indirect ophthalmoscopy (of the central and peripheral retina) and gonioscopy were performed.

Twenty patients met the above criteria and were followed up for a period of 6 months to 2 years. They represent the material for this report.

Results

There were 12 males and 8 females, their ages ranging from 53 to 89. The follow-up time was from 6 months to 2 years (1 patient was followed up for 3 years), with an average of 10·1 months per case (Table 1).

Table 1 *Follow-up time—cataract extraction with vitrectomy*

Months of follow-up	*No. of cases*
6	8
9	3
12	6
18	2
36	1
Average time	10·1

Table 2 reflects the comparative results in both eyes of the 20 patients. Seventeen patients retained useful vision (6/60 or better); 2 of them had a visual acuity in the eye after vitrectomy better than in the fellow eye with uneventful extraction, and 2 others ended up with equal vision in both eyes. In 6 patients the visual acuity in the eye with uncomplicated extraction was better by only 1 line on the Snellen chart.

Seven patients had a higher astigmatism in the eye with vitrectomy and 2 patients in the uneventfully operated upon eye, while the other 11 had either an equal amount of astigmatism or an astigmatism of less than 1 dioptre.

The final visual acuity and the amount of astigmatism were submitted to statistical analysis. With Student's t test no statistically significant differences could be found ($P>0{\cdot}1$) between the 2 groups of eyes.

The pupil was peaked or irregular in 7 eyes after vitrectomy and in 2 eyes after uncomplicated cataract extraction, while peripheral anterior synechiae of 45° or more were seen in 7 eyes after vitrectomy and in 3 of the eyes uneventfully operated on.

The main difference in the findings occurred in the posterior segment, where none of the straightforward operations developed any complications, while among the eyes after vitrectomy there were 2 patients with cystoid macular oedema, 3 others with vitreous opacities following haemorrhage, and 1 with retinal detachment which occurred 8 weeks after surgery.

Two patients developed glaucoma, in 1 patient complicated with bullous keratopathy which necessitated further surgery, but the patient did not regain useful vision. No cases of glaucoma were noted among the 20 eyes without vitrectomy.

In Table 3 it can be seen that, while the eyes without vitrectomy settled or had only slight discomfort 8 weeks after surgery, 7 eyes after vitrectomy still had mild to moderate irritation 3 months after surgery.

Discussion

The visual results in the eyes after vitrectomy in this report, though certainly inferior to those in the eyes not subjected to vitrectomy, compare favourably with the results quoted in the previous decade by Vail (1965, 1968) and more recently by Gardner (1975). The fact that Vail's patients were followed up for longer periods than ours cannot explain the difference in the results, as it is accepted that most of the complications attributed to vitreous loss occur during the first year after cataract surgery (Jaffe, 1972).

So far as the complications are concerned, it appears that cystoid macular oedema occurred less frequently in our patients than in other series (Cerasoli and Kasner, 1971; Gardner, 1975).

The final results in the anterior segment of the eyes with vitrectomy are quite satisfactory both in our and other authors' experience (Luntz, 1977; MacPherson, 1976). It is the posterior part of the eye where the major complications still occur, and

Table 2 *Final results in 20 patients with bilateral cataracts: uneventful surgery* (U); *anterior vitrectomy* (V)

Case no.	*Amount of astigmatism*		*Visual acuity*		*Pupil shape*		*AC angle*		*Fundus*		*IOP*		*Remarks*	
	U	V	U	V	U	V	U	V	U	V	U	V	U	V
1	1·0	1·0	6/5	6/24	R	P	N	N	N	Cystoid macular oedema	N	N	—	—
2	1·0	1·0	6/5	6/6	R	R	PAS	N	N	N	N	N	—	—
3	1·0	2·5	6/9	6/18	R	R	N	PAS	N	N	N	N	—	—
4	1·0	2·75	6/7·5	6/60	R	R	N	N	N	N	N	N	—	Opaque vit. haem.
5	1·0	1·0	6/9	6/18	R	R	N	N	N	Cystoid macular oedema	N	N	—	—
6	1·0	1·0	6/24	3/60	P	P	PAS	PAS	N	No view	N	N	Old corneal leucoma	Opaque vit. haem.
7	1·0	1·0	6/9	6/5	R	P	N	PAS	N	N	N	N	—	—
8	1·0	1·5	6/6	6/7·5	R	R	N	N	N	N	N	N	—	—
9	1·0	3·0	6/12	HM	R	P	N	PAS	N	No view	N	High	—	Bullous keratopathy
10	1·25	1·0	6/7·5	6/36	P	P	N	PAS	N	Cupped disc	N	High	—	—
11	1·0	1·0	6/6	6/9	R	R	N	N	N	N	N	N	—	—
12	1·0	1·5	6/12	6/15	R	R	N	N	N	N	N	N	Pre-exist. corneal opacities	Pre-exist. corneal opacities
13	1·0	1·0	6/12	6/60	R	R	PAS	N	N	N	N	N	—	Opaque vit. haem.
14	1·0	1·0	6/12	HM	R	R	N	N	N	Ret. detach.	N	N	—	—
15	2·0	1·5	6/12	6/9	R	P	N	PAS	N	N	N	N	—	—
16	1·0	1·0	6/9	6/15	R	R	N	N	N	N	N	N	—	—
17	1·0	1·0	6/15	6/15	R	R	N	N	N	N	N	N	Pre-exist. corneal opacities	Pre-exist. corneal opacities
18	1·0	1·0	6/12	6/12	R	R	N	N	N	N	N	N	—	—
19	1·0	1·0	6/9	6/36	R	P	N	PAS	N	N	N	N	—	—
20	2·0	3·0	6/12	6/15	R	R	N	N	N	N	N	N	—	—

R = Round. P = Peaked. N = Normal. PAS = Peripheral anterior synechiae. HM = Hand movements

Table 3 *General appearance of eyes in first 12 weeks after operation*

Injection photophobia discomfort	*2 weeks*		*4 weeks*		*8 weeks*		*12 weeks*	
	U	*V*	*U*	*V*	*U*	*V*	*U*	*V*
0	3	—	8	1	14	2	16	8
+	7	2	6	7	6	8	4	5
++	6	9	5	6	—	6	—	6
+++	3	5	1	6	—	4	—	1
++++	1	4	—	—	—	—	—	—

U = Uneventful surgery. V = Anterior vitrectomy. 0 = None. + = Slight. ++ = Mild. +++ = Moderate. ++++ = Severe

there were differences there between the vitrectomy eyes and the eyes with uneventful cataract surgery.

Glaucoma was encountered in 2 eyes out of the 7 with peripheral anterior synechiae after vitrectomy but in none of the 3 eyes with peripheral anterior synechiae after uneventful cataract extraction. As peripheral anterior synechiae were found in 47% of uneventful cataract extractions (Racz *et al.*, 1974) the glaucoma is probably not directly related to these synechiae in our 2 cases.

Vitreous opacity due to haemorrhage was the most frequent complication which affected 3 patients (15%) in their vitrectomised eye. This complication, although quite common after vitreous loss (Jaffe, 1972), is not reported among the complications in most of the follow-up studies on the outcome of anterior vitrectomy in the recent literature.

The main difference between the 2 eyes in this study was found in the length of time from operation and to when the eyes settled. Virtually all patients had a red eye and complained of discomfort in the eye with vitrectomy well after the fellow eye was already quiet and trouble-free. We attribute this to the prolonged vitritis which accompanies these cases.

There is no doubt in our minds that it is the routine use of the operating microscope for cataract surgery in general and anterior vitrectomy in particular which is responsible for the improvement in the fate of eyes with vitreous loss during surgery. Kasner (1973) wrote that 'The eye can get along without vitreous'. This is a rather strong statement. But, while the surgeon should make every effort to avoid loss of vitreous during cataract surgery, if this complication does occur the vitrectomy should be generous and performed with patience until the entire iris and pupil rest in a concave shape on the remnants of the vitreous. We agree with Gardner (1975) that if this regimen is followed there will be fewer peaked pupils too after vitrectomy.

We are grateful to Professor M. H. Luntz for his help and criticism, and to Mrs D. G. Livingston for help with the statistics.

References

Cerasoli, J. R., and Kasner, D. (1971). A follow-up study of vitreous loss during cataract surgery managed by anterior vitrectomy. *American Journal of Ophthalmology*, **71**, 1040–1043.

Gardner, R. C. (1975). Anterior vitrectomy. *Annals of Ophthalmology*, **7**, 723–726.

Gass, J. D. M. (1970). Management of vitreous loss after cataract. *Archives of Ophthalmology*, **83**, 319–323.

Jaffe, N. S. (1972). *Cataract Surgery and its Complications*, pp. 124–127. Mosby: St. Louis.

Kasner, D. (1968). Vitrectomy: a new approach to the management of vitreous. *Highlights of Ophthalmology*, **11**, 304–309.

Kasner, D. (1973). Vitreous loss during cataract surgery. *Transactions of the American Academy of Ophthalmology and Otolaryngology*, **77**, 184–185.

Luntz, M. H. (1977). Indikation, technik und resultate der vorderen vitrektomie. *Klinische Monatsblätter für Augenheilkunde*, **170**, 855–862.

McPherson, S. (1976). Management of vitreous loss after cataract extraction. In *Advances in Ophthalmology*, Vol. 33. Microsurgery of Cataracts, Vitreous and Astigmatism, pp. 172–174. Edited by D. Pierse and H. J. Kersley. Karger: Basel.

Maumenee, A. E. (1957). Symposium: Post-operative cataract complications III. Epithelial invasion of the anterior chamber, corneal edema, retinal detachment, anterior chamber hemorrhages, chages in the macula. *Transactions of the American Academy of Ophthalmology and Otolaryngology*, **61**, 51–68.

Mazjna, Y., and Miyake, K. (1972). Anterior vitrectomy: indication in vitreous loss during lens extraction. *Folia Ophthalmologica Japonica*, **23**, 22–26.

Racz, P., Szilvassy, I., and Pinter, E. (1974). The chamber angle after uneventful cataract extraction. *Klinische Monatsblätter für Augenheilkunde*, **164**, 218–220.

Uchino, M. (1975). A follow-up study of vitreous loss after cataract extraction. *Folia Ophthalmologica Japonica*, **26**, 479–482.

Vail, D. (1965). After results of vitreous loss. *American Journal of Ophthalmology*, **59**, 573–586.

Vail, D. (1968). Loss of vitreous during cataract surgery. *Highlights of Ophthalmology*, **11**, 107–119.

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Sclerotomy for pars plana vitrectomy

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SUMMARY A sclerotomy technique for vitreous surgery via the pars plana is described.

Closed vitrectomy has largely supplanted the 'open sky' method, particularly because it results in minimal interference with the integrity of the globe. Ideally the pars plana sclerotomy should be sufficiently watertight to allow the intraocular pressure to be maintained during surgery without impeding free movement of the vitrectomy instrument within the eye. We describe a sclerotomy technique for use with the Machemer VISC, Douvas Rotoextractor, and Peyman Vitrophage which achieves these objectives.

Method

A limbus-parallel incision 4 mm in length is made through half the thickness of the sclera 4·0 to 5·0 mm behind the limbus, and the central 2·5 mm deepened to expose the ciliary body (Fig. 1*a*). To obtain a circular opening into the vitreous cavity a knuckle of uveal tissue is prolapsed and abscised with de Wecker's scissors, and the anterior hyaloid or vitreous base is then incised in such a way that the opening into the gel is larger than the opening through the coats of the eye (Machemer, 1972; Peyman and Sanders, 1975).

Enlargement of the wound by stretching or splitting of the sclera during surgery is prevented by placing two 6–0 Dexon (polyglycollic acid) sutures across the sclerotomy at the margins of the full-thickness opening (Fig. 1*a*). The suture nearer to the surgeon is tied at this time because it is difficult for the assistant to do this once the instrument is in the eye. The vitreous cutter is then passed through the opening and the second suture tied in a bow (Fig. 1*b*).

At the end of the operation the infusion is turned off and no attempt made to close the wound round the instrument as it is withdrawn. The second suture is made fast and a third is placed across the middle of the opening (Fig. 1*c* and *d*). If necessary, the eye

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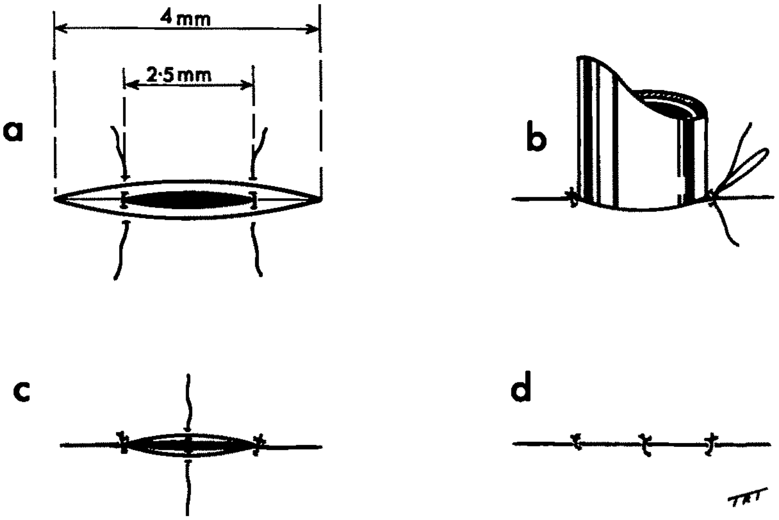

Fig. 1 *Pars plana sclerotomy*

can be reflated with infusion fluid injected through the closed incision.

Discussion

Several types of sclerotomy have been devised for closed vitrectomy. Stab incisions, using a knife whose width is exactly half the circumference of the vitreous cutter (Machemer, 1972) are associated with a high incidence of entry-site dialysis, probably due to inadequate incision of deep tissues (Machemer and Norton, 1972; Mandelcorn *et al.*, 1976).

Furthermore, limbus-parallel incisions, unguarded by sutures, stretch under the stress of prolonged surgery, allowing fluid to leak out of the eye around the instrument.

These problems do not arise with the Ocutome system of small openings for narrow instruments each performing a single function (O'Malley and Heintz, 1972). Similarly, when wider instruments are introduced, especially those whose diameter is increased by a fibreoptic sleeve, the problems appear to be minimised by using a trocar and cannula (Kloti, 1974). In our experience, however, this device restricts manoeuvrability and requires an excessively large opening in the globe.

A wide incision, controlled by a mattress suture, allows the surgeon adequate exposure to incise the deep tissues, and Peyman and Sanders (1975) report that in this way the risk of retinal dialysis is reduced to a minimum. However, control of the wound by a mattress suture is difficult to maintain throughout a long operation, and the heavy suture material required has to be replaced by a fine, absorbable suture at the end of surgery. The sclerotomy technique described above enables us to make an adequate opening in the deep structures while allowing effective control of the wound throughout surgery. Furthermore, closure is simple, requiring only a single additional suture.

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References

Kloti, R. (1974). Vitrectomy II. Surgical techniques with the vitreous stripper. *Albrecht von Graefes Archiv für klinische und experimentelle Ophthalmologie*, **189**, 125–135.

Machemer, R. (1972). A new concept for vitreous surgery: 2. Surgical techniques and complications. *American Journal of Ophthalmology*, **74**, 1022–1033.

Machemer, R., and Norton, E. W. D. (1972). A new concept for vitreous surgery: 3. Indications and results. *American Journal of Ophthalmology*, **74**, 1034–1056.

Mandelcorn, M. S., Blankenship, G., and Machemer, R. (1976). Pars plana vitrectomy for the management of severe diabetic retinopathy. *American Journal of Ophthalmology*, **81**, 561–570.

O'Malley, C., and Heintz, R. M. (1972). Vitrectomy via the pars plana: a new instrument system. *Transactions of the Pacific Coast Oto-Ophthalmological Society*, **53**, 121–137.

Peyman, G. A., and Sanders, D. R. (1975). *Advances in Uveal Surgery, Vitreous Surgery and the Treatment of Endophthalmitis*, pp. 128–130. Appleton-Century-Crofts: New York.

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Surgery of congenital and juvenile cataracts: a pars plicata approach with the vitrophage

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SUMMARY Eighteen eyes with congenital cataracts were surgically managed by pars plicata lensectomy and vitrectomy using the vitrophage. No major intraoperative or postoperative complications were encountered. All eyes have maintained extremely clear media, attached retinas, and absence of pupillary block during a follow-up period ranging from 12 to 36 months.

In the last two decades numerous advances have been made in the management of congenital cataracts. The intraoperative and postoperative complications associated with discission, linear extraction, and intracapsular lens extraction have been reduced with the re-introduction of the aspiration technique (Scheie, 1960). Development of phacoemulsification instruments (Kelman, 1967; Shock, 1974; Girard, 1974) greatly simplified the aspiration procedure. However, such postoperative complications as secondary membrane formation continue to occur with these techniques and require additional surgery (Hiles and Wallar, 1974; Hiles and Hurite, 1973).

With the use of automated vitrectomy instruments a new dimension has been added to the treatment of congenital cataracts. Surgical approach through the limbus (Calhoun and Harley, 1975) and pars plicata (Peyman *et al.*, 1977) has been described previously.

This report indicates our moderately long-term results in patients with congenital and juvenile cataracts who were managed with a pars plicata approach by combined lensectomy and vitrectomy using the vitrophage (Peyman and Sanders, 1975).

Material and methods

Seventeen patients (18 eyes) were referred for the management of congenital cataract to the Vitreous Service of the University of Illinois Eye and Ear Infirmary. In 14 patients the contralateral eye had been managed with other surgical techniques such as phacoemulsification and aspiration. In 1 patient both eyes were managed by pars plicata approach as described below. The other patients had no previous surgery, and only 1 eye of each was operated on. In 1 of these the cataract was unilateral, and the other patient refused operation on the fellow eye.

The patients' ages ranged from 6 months to 37 years. Three patients were 25 years or older and the remainder were 15 or younger (Table 1). Patients 3 and 5 are twins. In 4 patients the cataracts were due to maternal infection with rubella during pregnancy; in 2 patients the family history suggested autosomal dominant mode of inheritance; and in the remainder the aetiology was unknown. In all the eyes combined lensectomy and vitrectomy was performed by means of the vitrophage (Peyman and Sanders, 1975).

In children surgery was performed with the patient under general anaesthesia. In adults local (retrobulbar) anaesthesia was used. Initially an examination of both eyes is done before the standard surgical preparation is made. Traction sutures are then passed through both eyelids, followed by traction sutures under the insertion of the 4 rectus muscles, 4–0 black silk being used. After adequate exposure is obtained, a limbal peritomy, usually in the infratemporal quadrant, is made. In children a 4-mm-long sclerotomy is made 2·5 mm posterior and parallel to the limbus, a No. 15 Bard-Parker blade being used. In adults, however, the sclerotomy can be made 3·5 mm from the limbus.

The underlying ciliary body is cauterised or diathermised gently. A mattress suture of 5–0 polyglactin 910 or 4–0 Supramid is passed through the lips of the sclerotomy, and a double throw-knot is applied loosely. The suture material is then looped out of the sclerotomy. A 52-s Beaver blade is inserted through the sclerotomy into the lens and then removed with a slicing motion to widen the

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Table 1 *Patients treated with pars plicata lensectomy and vitrectomy*

Case no.	*Age*	*Aetiology and remarks*	*Complications*	*Approximate clarity of fundus view*
1	14 yr	Unknown	None	20/20
2	5 yr	Unknown	None	20/20
3	4 yr	Rubella syndrome, esotropia	None	20/20
4	4½ yr	Rubella syndrome	None	20/20
5	4 yr	Rubella syndrome	Transient corneal oedema postoperatively	20/20
6	1¼ yr	Unknown, esotropia	Self-limited bleeding from iris intraoperatively	20/20
7	6 mo	Autosomal dominant congenital cataract	Transient slight corneal haze postoperatively	20/20
8	6 mo	Autosomal dominant congenital cataract	None	20/20
9	4 yr	Rubella syndrome	None	20/20
10	10 mo	Unknown	None	20/20
11	2½ yr	Unknown	None	20/20
12	15 yr	Aniridia and nystagmus	None	20/20
13	25 yr	Chorioretinal scars	None	20/20
14	34 yr	Unknown	None	20/20
15	8 yr	Unknown	None	20/20
16	37 yr	Unknown, nystagmus	None	20/20
17	6 mo	Autosomal dominant congenital cataract	None	20/20
18	7 mo	Unknown	None	20/20

tract for insertion of the lens fragmentor. A lens fragmentor (Peyman and Sanders, 1975) is introduced into the lens through the sclerotomy, and the lens material is fragmented for about 60 seconds.

After this the lens fragmentor is removed and replaced with a wide-angle cutter vitrophage (Peyman, 1975). The mattress scleral suture is tightened round the vitrophage. The cortical and nuclear fragments are removed first, followed by the lens capsule. An anterior and a central vitrectomy is performed to the optic disc, after which the vitrophage is removed and the scleral mattress suture tied. The conjunctiva is sutured with 6–0 plain catgut. At the conclusion of the operation, antibiotic and cycloplegic eye drops are instilled.

In cases when the pupil does not dilate well sector iridectomy is performed with the vitrophage. The infusion fluid used for replacement of vitreous is 5% dextrose in 0·45% normal saline containing 2·2 g sodium bicarbonate and 0·2 g/litre calcium chloride. We routinely add 4 μg/ml of gentamicin of infusion fluid.

Results

No operative complications were encountered in 17 eyes. One eye (Patient 6, Table 1) had minimal bleeding from the iris, which stopped spontaneously.

During the early postoperative period transient corneal oedema, noticed in 2 patients' eyes, cleared over a period of 2 to 3 weeks. There was no evidence of intraoperative or postoperative bleeding at the site of entry into the pars plicata or development of retinal dialysis. Surgery was tolerated well, and there was no obvious difference between the eyes with rubella- and non-rubella-induced cataracts during the postoperative period.

Postoperatively the media were extremely clear (approximately 20/20 in clarity) in all eyes. As a majority of these patients have associated disorders such as amblyopia, microphthalmia, retinal scarring, or mental retardation, the final visual acuity was often difficult to assess.

No increase in intraocular pressure was noticed, and no severe or persistant intraocular inflammation appeared. No retinal detachment has been evident during the follow-up, ranging from 12 to 36 months. No case of pupillary block with shallow anterior chamber occurred.

Discussion

Management of congenital cataracts, a matter of great controversy, can be separated into three main areas of debate: the indication and timing of surgical intervention; the technical procedures of choice; and the management of amblyopia and postoperative optical correction. Our discussion will be confined to the technical aspects of congenital cataract surgery, although it is recognised that restoration of good visual function often depends on postoperative management and correction of amblyopia.

Despite the availability of various surgical techniques no one procedure has gained wide acceptance because of inherent complications associated with each. The simple discission technique had an unacceptable rate of complications such as swelling or retained lens matter, glaucoma, and retinal detachment (Barkan, 1932; Chandler, 1951; Cordes, 1956). Although better results have been reported with linear extraction (Owens and Hughes, 1948; Bagley, 1949), this technique was also associated with complications such as delayed formation of anterior chamber, anterior synechiae and updrawn pupil, occlusion of pupil, membrane formation, vitreous loss, glaucoma, and retinal detachment (Cordes, 1961). Similarly, intracapsular extraction produced complications in a very high percentage of cases (Ryan *et al.*, 1965) and was advocated by only a few surgeons (Escapini, 1968).

The aspiration techniques have greatly reduced the complications associated with older methods (Sheppard and Crawford, 1973). Although the incidence of postoperative glaucoma and retinal detachment was reduced significantly (Parks and Hiles, 1967; Ryan *et al.*, 1965; Ryan and von Noorden, 1971), secondary membrane formation and vitreous loss have continued to be major problems. Parks and Hiles (1967) reported a 73% incidence of membrane formation and 6% vitreous loss in a review of 52 eyes that underwent discission and aspiration. Ryan and von Noorden (1971) reported 23% incidence of secondary membrane and 8% vitreous loss in 75 cases by using the discission and the aspiration technique. The incidence of postoperative secondary membrane formation with aspiration techniques ranged from 18% (Sheppard and Crawford, 1973) to 73% (Parks and Hiles, 1967).

Although phacoemulsification has greatly facilitated the surgical management of congenital cataract surgery, complications such as vitreous loss and secondary membrane formation are still major problems that often require additional surgery (Hiles and Hurite, 1973). Hiles and Wallar (1974) reviewed their experiences with phacoemulsification and aspiration in infantile cataract surgery in 390 eyes. They reported secondary or delayed posterior capsulotomies in 66% of their aspiration group and 39% in their phacoemulsification group. A total of 70% of the eyes in the aspiration series required a capsulotomy either at the end of the operation or later. Of those eyes undergoing phacoemulsification 58% required a capsulotomy. Hiles (1977) states that as many as 92% of these children will need capsulotomies if enough time has elapsed after the original cataract surgery.

Automated vitrectomy instruments have greatly aided our ability to deal with secondary membrane and vitreous loss. Although we have advocated the pars plana approach for adult patients, we suggest the pars plicata approach for children. Anatomically the pars plana region is smaller in children than in adults. By making the sclerotomy 2·5 mm from the limbus and entering the eye through the pars plicata a safe distance from the ora serrata is maintained. Transillumination through the pupil is sometimes helpful in identifying the ciliary body.

The pars plicata approach offers many advantages over the limbal approach. With the limbal aproach Calhoun and Harley (1975) reported unplanned iridectomies in 14% of cases and a similar incidence of unexplained prolonged intraocular inflammation. The pars plicata route avoids direct manipulation of the corneal endothelium, and, similarly, contact with the iris is kept to a minimum. Any accidental bleeding from the iris into the deep vitreous can be treated immediately with the pars plicata approach, because a fundus contact lens can immediately be placed on the unmanipulated cornea. Moreover, lens particles that may fall into the vitreous can also be retrieved, so that the chance of postoperative inflammation is thus reduced. With the pars plicata approach the tip of the vitrophage can easily reach behind the iris and remove most of the lens material by applying only suction, a procedure which is rather difficult through the limbal approach, particularly in the axis of the shaft of the instrument.

In our series no patient has had severe intraocular inflammation postoperatively. We routinely remove the anterior vitreous with a central core of vitreous down to the optic disc. This technique has eliminated the development of pupillary block glaucoma.

Our patients have been followed up for periods ranging from 12 to 36 months. All eyes have maintained extremely clear media postoperatively. Using serial refraction measurements, we have been able to observe normal growth and development in these eyes when compared with contralateral eyes. With the evidence at hand we can postulate that pars plicata lensectomy and vitrectomy has no immediate untoward effect on the development of infant eyes. Although additional long-term results of this technique are clearly desirable, the present data are encouraging.

Combined pars plicata lensectomy and vitrectomy offers a 'one procedure' technique for the surgical management of congenital cataracts with minimal complications.

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References

Bagley, C. H. (1949). Congenital cataracts: a survey of the various types of operation. *American Journal of Ophthalmology*, 32, 441–419.

Barkan, O. (1932). A procedure for the extraction of congenital, soft and membranous cataracts. *American Journal of Ophthalmology*, 15, 117–124.

Calhoun, J. H., and Harley, R. D. (1975). The roto-extractor in pediatric ophthalmology. *Transactions of the American Ophthalmological Society*, 73, 292–305.

Chandler, P. A. (1951). Surgery of the lens in infancy and childhood. *Archives of Ophthalmology*, 45, 125–138.

Cordes, F. C. (1956). Failure in congenital cataract surgery: A study of fifty-six enucleated eyes. *Transactions of the American Academy of Ophthalmology and Otolaryngology*, **60**, 345–367.

Cordes, F. C. (1961). Linear extraction in congenital cataract surgery. *American Journal of Ophthalmology*, **52**, 355–367.

Escapini, H. (1968). Intracapsular extraction of congenital cataract. *American Journal of Ophthalmology*, **66**, 683–687.

Girard, L. J. (1974). Cataract extraction by ultrasonic aspiration, vitrectomy by ultrasonic aspiration. *Transactions of the American Academy of Ophthalmology and Otolaryngology*, **78**, 50–59.

Hiles, D. A. (1977). Phacoemulsification of infantile cataracts. *International Ophthalmology Clinics*, **17**, 83–102.

Hiles, D. A., and Hurite, F. G. (1973). Results of the first year's experience with phaco-emulsification. *American Journal of Ophthalmology*, **75**, 473–477.

Hiles, D. A., and Wallar, P. H. (1974). Phacoemulsification versus aspiration in infantile cataract surgery. *Ophthalmic Surgery*, **5**, 13–16.

Kelman, C. D. (1967). Phaco-emulsification and aspiration: a new technique of cataract removal: a preliminary report. *American Journal of Ophthalmology*, **64**, 23–35.

Owens, W. C., and Hughes, W. F. (1948). Results of surgical treatment of congenital cataract. *Archives of Ophthalmology*, **39**, 339–350.

Parks, M. M., and Hiles, D. A. (1967). Management of infantile cataracts. *American Journal of Ophthalmology*, **63**, 10–19.

Peyman, G. A. (1975). Wide-angle cutter vitrophage. *Ophthalmic Surgery*, **7**, 96–97.

Peyman, G. A., and Sanders, D. R. (1975). Modern methods of vitreous surgery. In *Advances of Uveal Surgery, Vitreous Surgery, and the Treatment of Endophthalmitis*, p. 113. Appleton-Century-Crofts: New York.

Peyman, G. A., Sanders, D. R., Marc, R., and Korey, M. (1977). Vitrophage in management of congenital cataracts. *Albrecht von Graefes Archives für Klinische und experimentelle Ophthalmologie*, **202**, 305–308.

Ryan, S. J., Blanton, F. M., and von Noorden, G. K. (1965). Surgery of congenital cataract. *American Journal of Ophthalmology*, **60**, 583–587.

Ryan, S. J., and von Noorden, G. K. (1971). Further observations on the aspiration technique in cataract surgery. *American Journal of Ophthalmology*, **71**, 626–630.

Scheie, H. G. (1960). Aspiration of congenital or soft cataracts: a new technique. *American Journal of Ophthalmology*, **50**, 1048–1056.

Sheppard, R. W., and Crawford, J. S. (1973). The treatment of congenital cataracts. *Survey of Ophthalmology*, **17**, 340–347.

Shock, J. P. (1974). Phacocryolysis combined with phacofragmentation and irrigation for removal of cataracts. *American Journal of Ophthalmology*, **77**, 860–864.

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The management of lens damage in perforating corneal lacerations

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SUMMARY Lens damage is present in 30% of perforating injuries of the anterior segment of the eye. There is no consensus on whether the cataractous lens should be removed at the initial repair of the corneal laceration or later, when the eye has recovered from injury. Twenty-seven consecutive cases with a perforating corneal injury and lens damage were alternatively treated either with simultaneous corneal suturing and cataract removal or with corneal suturing and delayed cataract removal several weeks later. The difference in the frequency of complications between the 2 groups was significant. The 1-step procedure was technically easier to perform, the period of postoperative irritation was shorter, complications due to the presence of an injured lens were prevented, and visual rehabilitation occurred earlier.

Lens damage is present in 30% of perforating ocular lacerations (Roper-Hall, 1959; Muga, 1975; Adhikary *et al.*, 1976). There are 2 ways of managing these cases: the immediate repair of the corneal laceration, leaving the cataract for a second operation as a separate problem; or the simultaneous corneal repair and extraction of the cataract. Some authors think that the cataract should be removed during the initial operation (Barraquer, 1975; Haik and Coles, 1972); others may prefer to wait and treat the cataract at a later stage after primary repair of the penetrating wound (Reinecke and Beyer, 1966; Havener and Gloeokner, 1969; Duke-Elder, 1972).

The purpose of this paper is to report our experience with the management of lens injury coexisting with perforating lacerations of the anterior segment of the eye.

Materials and methods

Between March and December 1976, 129 perforating injuries of the anterior segment were admitted to the Ophthalmology Service of the Dr Alejandro del Río General Emergency Hospital in Santiago, Chile. Thirty-eight cases had lens damage at slit-lamp examination. In 27 patients lens damage presented as a disruption of the capsule with or without herniation of some lens substance, but the lens maintained its body and normal location. These patients were consecutively and alternately included in 2 series. In one series the damaged lens was aspirated simultaneously with the wound repair and in the other series aspiration of the lens was deferred for a second operation. Eleven cases presented with a completely disrupted lens, with flocculent lens material dispersed in the anterior chamber or outside the wound. In 2 of these 11 cases the lens could not be identified. These patients presented also severe damage to posterior segment structures, vitreous and ciliary body. Lens material was eliminated during the anterior chamber toilet at first surgery. Only in 2 cases was the state of the lens not clear at first examination due to the presence of fibrin or exudate in front of the pupil. These cases were operated on for repair of the corneal wound and observed for lens damage. These last 2 groups were not included in the evaluation of the 2 series.

The results of the 2 series were analysed comparing the following parameters: anterior chamber activity, iris synechiae to the wound or the lens remnants, fibrous strands in the anterior segment, anterior chamber depth, and complications. Final vision was not considered to evaluate the 2 series, since many effects of ocular trauma other than lens damage influence the final results. However, it will be presented in the tables.

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Table 1 *Simultaneous aspiration of the lens and corneal wound repair*

Case no.	*Age (years)*	*Interval injury to operation (hours)*	*Postoperative evaluation* *Anterior chamber*	*Sinechiae*	*Ocular irritation (days)*	*Complications*	*Vision*
1	7	4	Flat	None	3	Pupillary block	20/70
2	13	2	Deep	None	4	Lens remnants	20/50
3	14	4	Deep	None	5	None	NLP
4	27	12	Deep	+	4	None	HM
5	13	19	Deep	None	4	None	20/70
6	7	2	Deep	None	5	Hyphaema	20/100
7	4	7	Deep	None	4	None	—
8	15	48	Deep	None	9	None	20/30
9	19	42	Deep	None	5	None	20/70
10	27	4	Deep	None	4	None	20/70
11	21	4	Deep	None	5	None	20/25
12	28	6	Deep	None	6	None	20/50

SURGICAL TECHNIQUE

The corneal laceration was repaired as previously described (Maul and Muga, 1977). When the injured lens was removed at the initial operation, it was aspirated and irrigated through two limbal keratotomies, not through the wound. Two 20-gauge cannulas were used, 1 connected to the anterior chamber with a Ringer's solution reservoir and the other connected to the anterior chamber with a vacuum pump. The anterior chamber depth was maintained with saline perfusion during the operation. In the other series at initial surgery the wound was sutured and the anterior chamber reformed. Six weeks later the patients were rescheduled for cataract surgery. An aspiration and irrigation technique as described was used. In both series a peripheral iridectomy was performed and the anterior chamber was reformed with saline and air and swept with a cyclodialysis spatula for prevention of sinechiae.

Results

In Table 1 the results of simultaneous aspiration of the lens and repair of the corneal laceration in 12 patients is presented. In 15 cases aspiration of the lens was programmed to be done 6 weeks later. However, in 10 of these lens surgery had to be performed earlier. In Table 2 the features of these 10 cases are given. Between 1 and 8 days from the first operation of these cases the cataract became intumescent and an immediate removal was necessary. This is a high percentage of early emergency reoperations and does not agree with a waiting period of 3 to 4 weeks. In Table 3 the features of 5 cases where surgery was done 6 weeks after primary repair are presented. All patients received systemic antibiotics. Atropine 1% and antibiotic-steroid eyedrops were administered in the conjunctival cul-de-sac.

Aspiration of disrupted lens at initial repair in our series offered the following advantages: lens substance was easily aspirated, transparency of the freshly lacerated cornea allowed good observation of anterior segment structures, and manipulation of tissues was easy to control. Mixture of lens material and vitreous was avoided, which if associated with hyphaema may turn the situation even worse (Coles and Haik, 1972; Hutton *et al.*, 1976). Postoperative anterior chamber activity was shorter. In cases where lens aspiration was done 6 weeks after primary repair of the corneal injury the following difficulties were encountered. Hardening of lens capsule and partially reabsorpted lens substance made its removal difficult. Synechiae of iris to the site of capsular disruption were always present. Vascularisation of lens substance and fibrous strands between anterior chamber structures were also a common finding. All these features determined a difficult and prolonged operation. Extraction of the lens could not be always completed, and hyphaema was a common complication.

Discussion

Simultaneous repair of a perforating injury of the

Table 2 *Corneal wound repair and early aspiration of the lens*

Case no.	Age (years)	Interval injury to wound repair (hours)	Interval wound repair to lens aspiration (days)	Cause of early reoperation*	Postoperative evaluation: Anterior chamber	Sinechiae	Ocular irritation (days)	Complications	Vision
1	9	1	1	*a*	Deep	+	4	None	—
2	6	30	8	*a, b*	Flat	–	18	—	20/200
3	21	2	6	*a*	Deep	–	10	None	—
4	7	17	1	*a*	Deep	+	9	None	20/400
5	52	20	5	*a, b*	Deep	–	11	None	20/400
6	5	4	4	*a, b, c*	Deep	–	11	None	20/100
7	9	6	1	*a*	Deep	–	4	None	20/100
8	50	4	7	*a*	Deep	–	14	None	20/70
9	8	6	1	*a*	Deep	–	7	None	20/70
10	22	7	28	*a*	Deep	–	16	None	20/50

* (*a*) Intumescent lens. (*b*) Flat anterior chamber. (*c*) Glaucoma

cornea and extraction of a coexisting injured lens allows restoration of anterior segment physiology at the first operation. There is less need for manipulation, the postoperative irritative period and anterior chamber activity is shorter, complications due to the presence of an injured lens are prevented, the number of reoperations is reduced, and visual rehabilitation occurs earlier.

When analysing lens damage after perforating injuries of the eye several categories of damage may be established. One relates to the degree of lens damage and another relates to presence or absence of additional damage to other intraocular structures. Where the lens capsule is severely disrupted and flocculent lens material is dispersed in the anterior chamber there is a general consensus that all lens material should be removed at the initial repair of the injured globe (Roper-Hall, 1959; Muga, 1975; Eagling, 1976). Where capsular damage is smaller and the cataractous lens maintains its body and position, removal of the cataract at initial repair has not been always done or recommended. The problems associated with the presence of an injured lens in an eye that has had a perforating injury repaired have recently been emphasised. The cataract may become intumescent, and lens endothelial contact, flattening of the anterior chamber, or phacomorphic glaucoma may develop (Maul and Muga, 1977).

Phacoanaphylaxis occurs commonly after ocular trauma associated with lens capsule disruption. It may develop as early as 1 to 14 days, leading the

Table 3 *Corneal wound repair and delayed aspiration of the lens*

Case no.	Age (years)	Interval injury to wound repair (hours)	Interval wound repair to lens aspiration (days)	Postoperative evaluation: Anterior chamber	Sinechiae	Ocular irritation (days)	Complications	Vision
1	22	72	44	Deep	+	16	Hyphaema, vascularisation of lens	HM
2	12	16	48	Deep	None	7	None	20/100
3	2	4	45	Deep	++	15	Hyphaema, vascularisation of lens	HM
4	13	47	47	Deep	+	16	Hyphaema, vascularisation of lens, fibrous lens capsule remnants	HM
5	6	8	30	Deep	+	14	Fibrous lens capsule remnants	20/200

eye to a state of chronic inflammation unless a total surgical removal of the lens is performed (Perlman and Albert, 1977). The need for control of inflammation in the follow-up of cases with a perforating injury is particularly important to prevent the development of synechiae, fibrous strands, or fibrous ingrowth (Coles and Haik, 1972; Hutton *et al.*, 1976). We may further add from the analysis of the present series that where lens surgery is deferred for a second operation several weeks later complications may be the rule.

Hyphaema occurred in 3 of 5 cases (see Table 3). Synechiae occurred very often, and the postoperative anterior chamber activity lasted 2 weeks. Ten cases in which lens aspiration was planned to be done 6 weeks after the initial repair of the corneal wound had to be operated on earlier because they developed an intumescence of the cataract soon after primary repair (see Table 2). In cases where cataract aspiration was done at initial repair of the globe postoperative complications were an exception, and ocular irritation and anterior chamber activity lasted only 5 to 6 days (see Table 1).

Removal of the lens in these cases was technically easy to perform. Transparency of the freshly lacerated cornea allowed optimal observation of anterior chamber structures. Anterior chamber depth, pupil area, and lens substance were perfectly seen through the microscope. Lens substance and capsular fragments offered no resistance to aspiration, and one could choose the intraocular structure to be manipulated, thus avoiding additional trauma during surgery.

Timing of lens surgery in our series influenced final results. Postoperative complications were less frequent and ocular irritation was shorter in duration in patients where simultaneous aspiration of the lens was performed as opposed to those reoperated upon later for removal of the cataract.

When associated damage of lens and other intraocular structures exist, the present trend in the management of such cases also favours a 'radical' primary surgical approach. This is specially valid for the presence of vitreous loss, since lens material mixed with vitreous fluid seems particularly devastating (Coleman and Franzen, 1974). Immediate removal of lens material and anterior vitrectomy has been recommended in such cases (Faulborn *et al.*, 1977). However, we think in the face of our results and that of others (Eagling, 1975) that a major role in later complications is played by the presence of an injured lens in such cases.

In any case of injury the final result will depend not only upon the injury itself and the initial damage but on the chosen method of treatment as well as on later complications, which in some instance may be influenced by prophylactic treatment (Roper-Hall, 1969). We think that a definitive treatment should be attempted for the laceration of the cornea or sclera as well as for the laceration of intraocular structures at primary repair.

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References

Adhikary, H. P., Taylor, P., and Fitzmaurice, D. J. (1976). Prognosis of perforating eye injury. *British Journal of Ophthalmology*, **60**, 737–739.

Barraquer, J. (1975). Personal Communication at the X Chilean Congress of Ophthalmology. Arica, Chile.

Coleman, D. J., and Franzen, L. A. (1974). Vitreous Surgery: Preoperative evaluation and prognostic value of ultrasonic display of vitreous hemorrhage. *Archives of Ophthalmology*, **92**, 375–379.

Coles, W. H., and Haik, G. M. (1972). Vitrectomy in intraocular trauma. Its rationale and its indications and limitations. *Archives of Ophthalmology*, **87**, 621–628.

Duke-Elder, Sir S. E. (1972). Injuries Part I. Mechanical injuries. *System of Ophthalmology*, Vol. 14, p. 351. Mosby: St. Louis.

Eagling, E. M. (1975). Perforating injuries involving the posterior segment. *Transactions of the Ophthalmological Societies of the United Kingdom*, **95**, 335–339.

Eagling, E. M. (1976). Perforating injuries of the eye. *British Journal of Ophthalmology*, **60**, 732–735.

Faulborn, J., Atkinson, A., and Oliver, D. (1977). Primary vitrectomy as a preventive surgical procedure in the treatment of severely injured eyes. *British Journal of Ophthalmology*, **61**, 202–208.

Haik, G. M., and Coles, W. H. (1972). Associated injuries of the iris and the lens. In *Intraocular Injuries*, p. 54. Lea & Febiger: Philadelphia.

Havener and Gloeokner (1969). *Atlas of Diagnostic Techniques and Treatment of Intraocular Foreign Bodies*, p. 34. Mosby: St. Louis.

Hutton, W. L., Snyder, W. B., and Vaiser, A. (1976). Vitrectomy in the treatment of ocular perforating injuries. *American Journal of Ophthalmology*, **81**, 733–739.

Maul, E., and Muga, R. P. (1977). Anterior segment surgery early after corneal wound repair. *British Journal of Ophthalmology*, **61**, 782–784.

Muga, R. P. (1975). Experiencia en el tratamiento de las heridas perforantes oculares. *Archivos Chilenos de Oftalmología*, **32**, 73–78.

Perlman, E. M., and Albert, D. M. (1977). Clinically unsuspected phacoanaphylaxis after ocular trauma. *Archives of Ophthalmology*, **95**, 244–246.

Reinecke, R. D., and Beyer, Ch. K. (1966). Lacerated corneas and prevention of sinechiae. *American Journal of Ophthalmology*, **61**, 131–135.

Roper-Hall, M. J. (1959). The treatment of ocular injuries. *Transactions of the Ophthalmological Societies of the United Kingdom*, **79**, 57–69.

Roper-Hall, M. J. (1969). A retrospective study of eye injuries. *Ophthalmologica*, **158**, 12–27.

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Aspiration from the vitreous of a non-magnetic foreign body

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SUMMARY A non-magnetic vitreal foreign body was aspirated from over the macula through the pars plana. The surgeon guided a blunt needle towards the foreign body while watching both with the binocular indirect ophthalmoscope. His assistant's tentative suction movements with an attached syringe drew the foreign body up into the needle without risking a retinal perforation. Visual recovery was complete. It is suggested that aspiration might be the procedure of choice for such small visible intraocular fragments.

A non-magnetic foreign body in the vitreous presents a difficult and dangerous clinical dilemma, since the foreign body itself and the surgical attempt to remove it may both bring about destruction of the eye. Neubauer (1963) originally described aspiration of such a foreign body through a special spoon-shaped cannula under direct vision and through an adjacent sclerotomy. More recently (Neubauer, 1975) he has advocated removal through the pars plana of freely moving vitreal foreign bodies, directly viewed with the ophthalmoscope.

We have aspirated a brass foreign body from over the macula while monitoring the intaocular manipulations with a binocular indirect ophthalmoscope. We entered the eye through the pars plana and used a standard blunt-ended 16 gauge needle attached to a standard disposable syringe. At the time we could not find any reports that might have given us the benefit of earlier experiences with such an approach. The perils of leaving a copper-rich alloy within the eye have been sufficiently well documented to convince us that surgical removal was necessary.

Case report

In August 1975 a 28-year-old man suffered a right partial hyphaema when he was struck on the eye by a shotgun cartridge. The visual acuity, surprisingly, was 6/6. No fundal view was possible, but routine *x*-ray examination was negative. After 2 days' bed rest the hyphaema subsided sufficiently to reveal a glistening 'golden' object over the macular area (Fig. 1). The patient in fact noticed its presence before we did. We presumed it to be a piece of the cartridge case, made of brass with a high copper content, and the gunmakers confirmed a level of 80% before we proceeded with the operation.

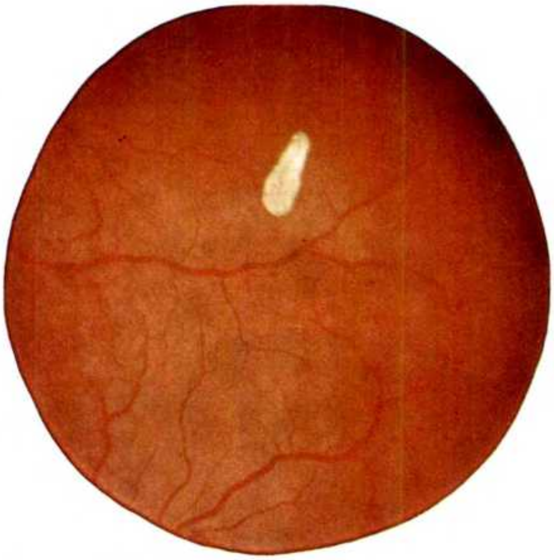

Fig. 1 *'Golden' object over macular area*

Under general anaesthesia the conjunctiva was opened along the limbus between the 7 and 11 o'clock meridians. A superficial foreign body was removed, and a penetrating entry wound was discovered just anterior to the scleral landmark of the ora serrata. Stay sutures were placed round all four rectus muscles to allow the assistant to tether

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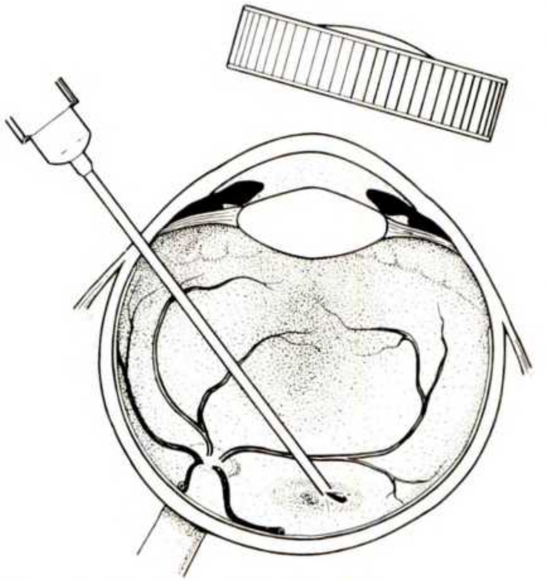

Fig. 2 *Foreign body sucked into needle*

the eye in any required position. The entry wound was now extended anteriorly for 1 mm and diathermy applied to the pars plana of the ciliary body deep to this opening. While the surgeon introduced the aspiration needle towards the macula, which he kept under continuous view with the indirect ophthalmoscope, the assistant, on his instructions, carried out tentative suction movements with the plunger of the syringe. When the blunt needle was within 2 mm of the foreign body, these movements sucked it into the stem of the needle (Fig. 2). The needle was removed at once, and the sclerotomy over the pars plana sutured with 5/0 PTFE coated polyester and the conjunctiva with catgut. A metal sliver 1·5 × 0·5 mm was then expelled from the needle.

The patient was kept in bed for the next day or so because there had been a small haemorrhage caused by the foreign body at the point of entry. This cleared up very quickly. A short course of systemic antibiotics was given, together with local mydriatics and local steroids.

His recovery was uneventful, and 2 years later the vision in the right eye is actually better than that of the left, now being 6/5. There is no evidence of vitreal disturbance, and the eye has clearly been undisturbed by this remarkably gentle invasion through the pars plana.

Discussion

No matter what the operative problem may be, surgical simplicity in both instrumentation and technique has much to commend it. In these particular circumstances, provided a foreign body is small and can be seen (larger fragments usually disappear into vitreal haemorrhage), all that is required is a routine intraocular surgical tray, a blunt-ended 16 gauge aspiration needle, a disposable syringe, and mastery of the indirect ophthalmoscope.

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References

Neubauer, H. (1963). The removal of non magnetic foreign bodies in the vitreous by aspiration. *Transactions of the Ophthalmological Societies of the United Kingdom*, **83**, 143–151.

Neubauer, H. (1975). Intraocular foreign bodies. *Transactions of the Ophthalmological Societies of the United Kingdom*, **95**, 496–501.

British Journal of Ophthalmology, 1978, **62**, 790–791

A disposable cannula for the aspiration of soft lens matter

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SUMMARY A double cannula is described suitable for the aspiration of soft lens matter. The cannula is a modification of a double irrigation needle already marketed and will be available in a presterilised disposable pack for use with disposable syringes.

Aspiration of lens matter (Scheie, 1960) is now generally accepted to be the method of choice when treating congenital cataracts as well as those in young adults when the nucleus is not sufficiently dense to cause problems. Many types of instrument have been devised for the operation. Many of them have been concerned with precise replacement of the volume of fluid aspirated in order to avoid loss of the anterior chamber (Fink and Weinstein, 1964; Atchoo, 1968; Phillips and Wang, 1971). With the use of the operating microscope equipped with an observer's viewing eyepiece and with the help of a competent assistant it is quite possible to maintain the depth of the anterior chamber throughout by syringing fluid gently into the anterior chamber with one syringe while at the same time aspirating fluid and lens matter with another (Ferguson, 1964; Girard, 1967; O'Gawa, 1967; Bruun-Jensen, 1969; Rice, 1977).

The purpose of this brief account is to describe a disposable double cannula, shortly to be available in prepacked and sterilised form, which can be used in conjunction with disposable syringes in everyday use.

The cannula is a modification of a disposable double cannula already available. It consists of a double pair of rounded off 'green' disposable needles, fused together, one needle being set back upon the other (Fig. 1). The longer of the 2 needles is attached to a disposable 2 ml syringe by means of a Luer fitting. The shorter of the 2 needles is attached to a length of soft Silastic tubing, about 6 in (15 cm) long, which fits on to a straight blunted needle of the same gauge and via a Luer fitting to the second syringe.

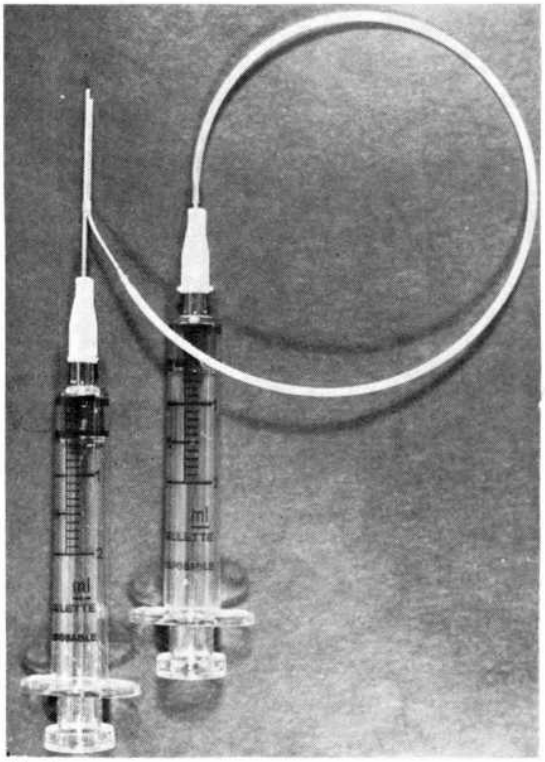

Fig. 1

It is possible to use a drip bottle attached directly to the shorter needle, but the latter is more bulky, and, the tubing being thicker, this tends to make delicate movements of the cannula within the eye more difficult. Maintaining sterility is also more difficult.

Method

The whole operation is performed through a single incision. The pupil is as widely dilated as possible,

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as for any aspiration procedure. An iridectomy is not necessary. A small incision about 2 mm long is made through the corneal side of the limbus at either the 12 o'clock position or temporally. It is important that this incision is not made too large lest fluid escape around the cannula and maintainance of the anterior chamber be difficult. If desired a U suture as described by Worst (1964) can be employed, but slight leakage is advantageous in preventing excessive inflow pressure. A disposable needle which has been 'hooked' at its point is passed into the anterior chamber and incises the anterior capsule. This needle is removed and the double needle inserted. Lens matter is gently aspirated while the assistant maintains the depth of the anterior chamber by observing through the assistant's eyepiece and using the inflow syringe.

Lens matter is aspirated quite quickly, the only difficult area being the equator of the lens beneath the cannula, but this can usually be dealt with as the cannula is withdrawn. The incision does not usually need to be sutured. Opinion is divided on the merits of using separate cannulae with 2 small incisions into the eye or a double cannula with a single slightly larger incision. The larger incision usually heals without complication, and a buried 10·0 monofilament nylon suture can be employed if necessary. Control of the input cannula in the former arrangement can be troublesome, because it is often just outside the microscope field and it is also liable to come out of the eye, especially if fine-bore tubing is used (Rice, 1977). For these reasons the double cannula described would seem to be the simplest and most convenient of the arrangements so far employed.

Messrs Needle Industries of Redditch made the cannula available.

References

Atchoo, P. D. (1968). Double barrel anterior chamber irrigating needle. *Archives of Ophthalmology*, **79**, 580–581.

Bruun-Jensen, J. (1969). Cataract aspiration-irrigation with twin needle. *Acta Ophthalmologia*, **47**, 498–501.

Ferguson, E. C. (1964). A modified instrument for aspiration and irrigation of congenital of soft cataracts. *American Journal of Ophthalmology*, **27**, 596–599.

Fink, A. I., and Weinstein, G. W. (1964). A modification of the Fuch's syringe. *American Journal of Ophthalmology*, **58**, 129–130.

Girard, L. J. (1967). Aspiration-irrigation of congenital and traumatic cataracts. *Archives of Ophthalmology*, **77**, 387–391.

O'Gawa, G. M. (1967). Double-bore cataract aspiration needle. *American Journal of Ophthalmology*, **64**, 970–971.

Phillips, C. I., and Wang, M. K. (1971). Cataract aspiration-irrigation. *British Journal of Ophthalmology*, **55**, 361–367.

Rice, N. S. C. (1977). Lens aspiration. *Transactions of the Ophthalmological Societies of the United Kingdom*, **97**, 48–51.

Scheie, H. (1960). Aspiration of congenital or soft cataracts: A new technique. *American Journal of Ophthalmology*, **50**, 1048–1055.

Worst, J. G. F. (1964). Goniotomy. *American Journal of Ophthalmology*, **57**, 185–200.

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Morphological changes in the human conjunctival epithelium. I. In the normal elderly population

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SUMMARY Forty-nine biopsies of bulbar conjunctiva from patients with no apparent conjunctival disease were studied by light and transmission electron microscopy. No significant morphological changes were recorded in those specimens from patients less than 79 years old. However, in the older age group the epithelium showed irregularities in thickness, a reduction in the goblet cell population, and in 25% the presence of 'hyaline bodies'. The epithelial irregularities consisted of mild superficial stratification, which was observed also in a few of the specimens from the younger age groups. The goblet cells appeared morphologically normal in all age groups. The significance of the hyaline bodies and their possible relationship to goblet cells is discussed.

Clinical studies have shown that tear secretion decreases in quantity and quality in the later decade of life, and mild keratoconjunctivitis sicca (KCS) can be identified in approximately 15% of people over the age of 80 years (Whaley *et al.*, 1972). Accordingly, it is possible that there are significant morphological changes in the conjunctival epithelium of the elderly, and it is important that these changes be documented to provide the necessary background information for the study of the conjunctiva in KCS (part II of this communication). This part of the report describes the light and electron microscope findings in the conjunctiva of a group of elderly persons.

Materials and methods

Forty-nine conjunctival biopsies from patients without apparent conjunctival disease were obtained during the course of routine cataract surgery. The operations were performed using retrobulbar injection of 1·5 ml lignocaine and with local instillation of 0·4% oxybuprocaine HCl drops. The details of the sex and age distribution of the group are shown in Table 1.

Table 1 *Distribution of patients according to age and sex*

Age (years)	*Male*	*Female*	*Total**
50–59	1	3	4 (3)
60–69	3	7	10 (5)
70–79	5	14	19 (8)
80–89	3	13	16 (9)
Total	12	37	49 (25)

*The figures in parentheses indicate the number of biopsies studies by electron microscopy

The biopsies, which were approximately 5 mm in diameter, were removed from the upper bulbar conjunctiva at a consistent site which was 5 mm from the limbus. Some of the biopsies were laid out on filter paper before fixation, but the majority were immersed immediately in 4% phosphate buffered glutaraldehyde. The latter technique was found to be preferable because stretching of the tissues on to the filter paper introduced artefactual damage to the epithelium.

Each specimen was then divided: half was processed for light microscopy, the other half for conventional transmission electron microscopy.

LIGHT MICROSCOPY

Qualitative assessment. The sections which were prepared from paraffin-embedded blocks were stained with haematoxylin and eosin, PAS, and orcein stains and were coded and assessed with regard to the following features: (1) Changes in the arrangement of the epithelial cells; (2) changes in

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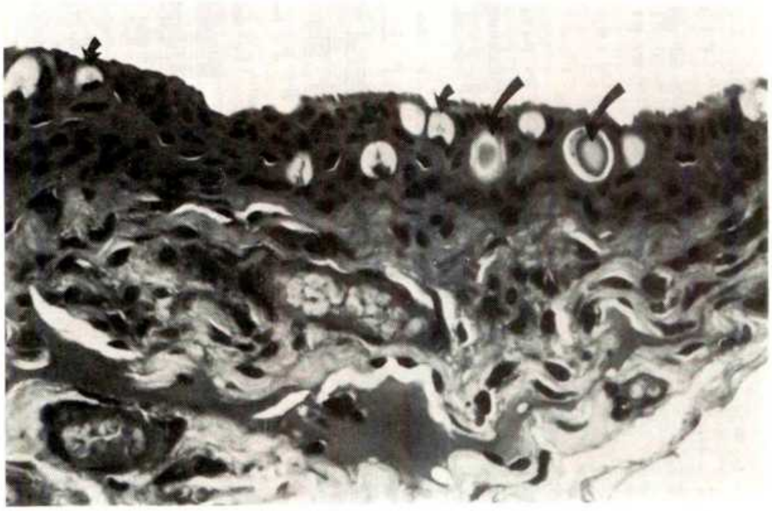

Fig. 1 *Light micrograph to show 'hyaline bodies' (large arrows) in a segment of epithelium which also contains goblet cells (small arrows). H. and E., ×385*

the morphology and arrangement of goblet cells; (3) changes in the inflammatory cell content of the conjunctival stroma.

Quantitative assessment of goblet cell. A count of epithelial goblet cells was performed on PAS-stained sections by means of a calibrated eyepiece graticule and a ×10 objective in a Leitz HM LUX light microscope. The number of goblet cells was expressed as the frequency per mm length of epithelium.

TRANSMISSION ELECTRON MICROSCOPY

The glutaraldehyde-fixed specimens were postfixed in 2% phosphate buffered osmium-tetroxide, passed through ascending grades of alcohol, and finally embedded in Araldite. Semithin (1 μ) and ultrathin (500 Å [50 nm]) sections were then cut on an LKB Ultrotome III. The semithin sections were stained with toluidine blue and were used for orientation. The ultrathin sections were double stained with uranyl acetate and lead citrate and were examined in the Phillips 301 EM.

Results

LIGHT MICROSCOPY

Qualitative assessment

The specimens were examined without prior knowledge of the age and sex of the patients. Significant alterations were found only in the epithelium of those over 80 years, so that the results can be presented in two parts.

(1) *Persons under* 80 *years.* The conjunctival epithelial morphology was identical with the established descriptions in the literature (Wolfe, 1967). There were no significant changes in the epithelial thickness or in the arrangement of the cells. The normal human bulbar conjunctiva in the region examined consisted of a 5- or more polyhedral non-keratinised epithelium with a basal cubical layer which lay above a folded basement membrane. Goblet cells were usually present in the superficial layers, and they tended to occur in aggregates, so that some epithelial segments contained more goblet cells than others.

(2) *Persons over* 80 *years.* The following features were of significance: *(i)* Variation in the epithelial thickness. This was seen as mild atrophy in some biopsies and an apparent but mild degree of hyperplasia in others. However, in all the specimens examined these irregularities tended to be focal, and long segments of epithelium of normal thickness alternated with the atrophic or hyperplastic areas. *(ii)* Abnormal structures in the epithelium; 'hyaline bodies'. In 4 of the 16 biopsies taken from persons (2 male and 2 female) over 80 years old, round or ovoid acellular structures were identified (Fig. 1). These were present in the superficial layers and were much larger than the adjacent goblet cells. They stained positively with the PAS stain and their content, unlike that of the goblet cells, was homogeneous. For convenience they were classified as being of a hyaline nature. *(iii)* Inflammatory cells, lymphocytes, plasma cells, and polymorphonuclear leucocytes were identified in the stroma and in the epithelium in this group of biopsies, but in distribution and number there was no significant pattern and no difference could be detected between the over- and the under-80s.

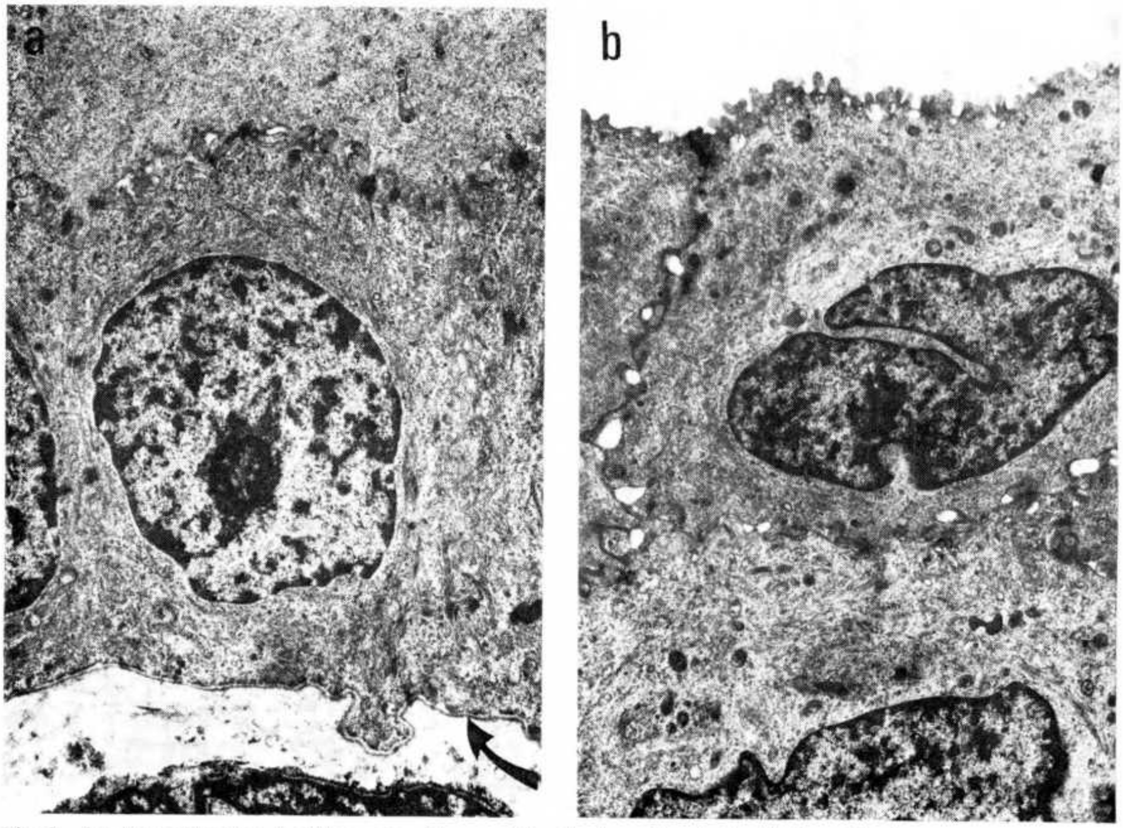

Fig. 2 *(a) The cubical basal cell layer in a 62-year-old patient's conjunctival epithelium. The basement membrane is shown by an arrow (× 6800). (b) The polygonal superficial cells in the conjunctival epithelium of the same individual. Note the wide intercellular spaces between the cells in this layer (× 6800)*

Quantitative assessment

The results obtained in the goblet cell count are shown in Table 2. In the group aged 50 to 79 the mean value (±SD) was 10±4 goblet cells/mm, with no significant statistical difference in the 3 age groups shown. However, in the group over 80 years the mean goblet cell count (±SD) was 16±3 goblet cells/mm, and this is significantly lower than that in younger age groups ($P<0{\cdot}05$). The observer error in this analysis was less than 5%.

Table 2 *Goblet cell count in the conjunctival epithelium according to age*

Age (years)	*Number of biopsies*	*Goblet cell/mm ± SD*
50–59	4	10·2 ± 3·5
60–69	10	10·2 ± 4
70–79	19	9·4 ± 3·8
80–89	16	6·4 ± 3

ELECTRON MICROSCOPY

Twenty-five biopsies were studied by transmission electron microscopy (Table 1). The morphology of the palpebral conjunctival epithelium has been described by Wanko *et al.* (1964), so that it is only necessary to outline the basic structure of the 3 cell layers and to emphasise the changes in structure which may be related to the ageing process. The essential morphological features of the epithelium were as follows.

Basal cells

The basal cell layer consisted of cubical cells which had a large ovoid nucleus in which nucleoli were prominent. The cytoplasm was rich in tonofibrils, but mitochondria, Golgi material, and rough endoplasmic reticulum were sparse and tended to be located in the perinuclear region (Fig. 2*a*). The tonofibrils were condensed and formed linear bundles (Fig. 3*a*), particularly in relation to the desmosome attachments, but this was less noticeable in the region of the hemidesmosomes at the base of

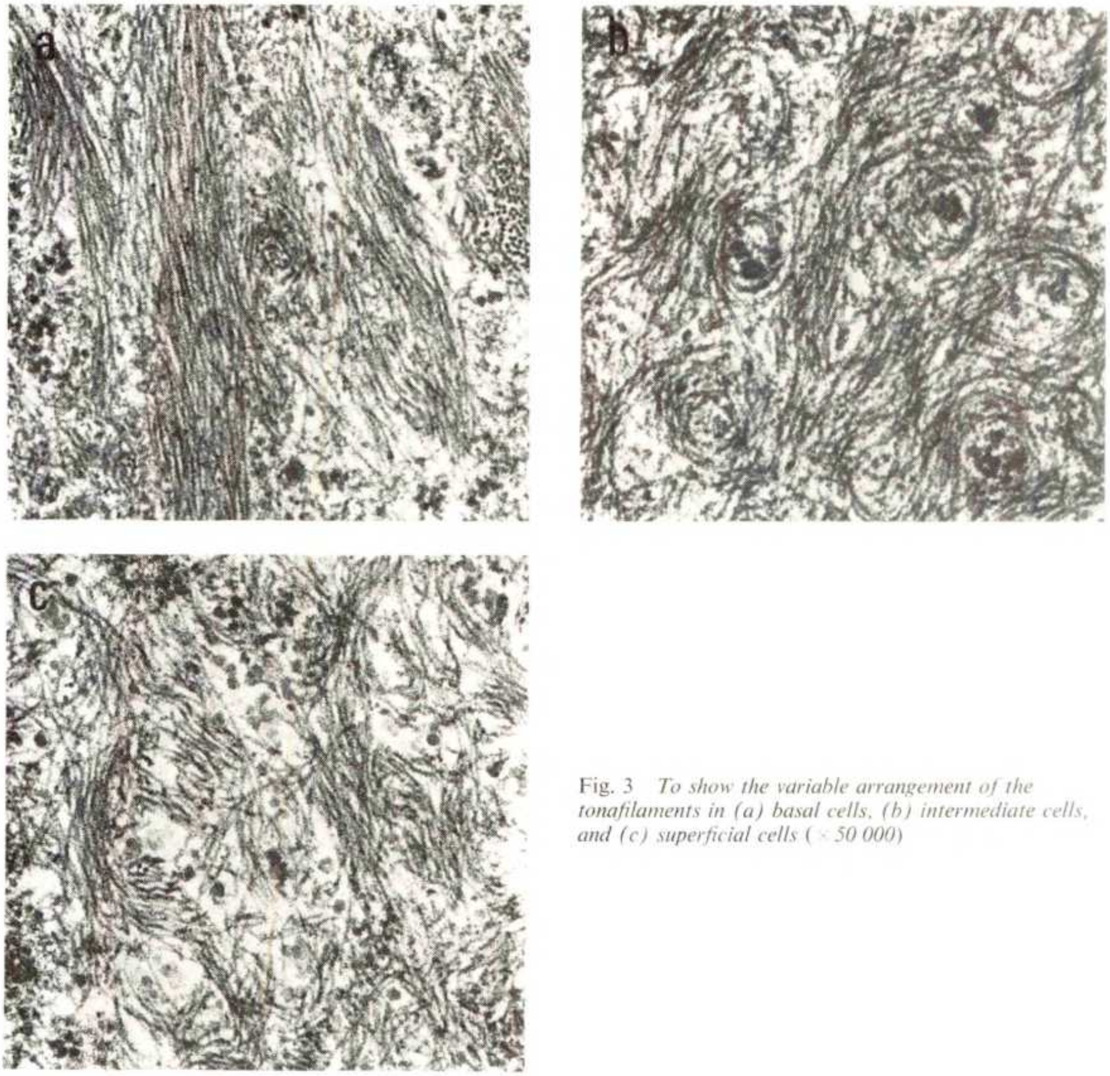

Fig. 3 *To show the variable arrangement of the tonafilaments in (a) basal cells, (b) intermediate cells, and (c) superficial cells* (× 50 000)

the cell. The cell membrane at the apex was undulating, and, although complex interdigitations were formed, the intercellular spaces were wide in this zone. The basement membrane formed a continuous electron-dense feltwork of fine filaments with some condensation in the region of the hemidesmosomes (Fig. 2*a*). Throughout the age range the morphological features of this layer were identical.

Intermediate cells

These consisted of polygonal cells with a less condensed cytoplasm than the basal layer. The organelle content was basically the same as that of the basal layer, except, that the mitochondria were larger, more electron-dense, and were dispersed evenly throughout the cytoplasm (Fig. 2*b*). The tonofibrils were arranged as interwoven bundles which surrounded clumps of ribosomes or glycogen granules (Fig. 3*b*). The intercellular space was tortuous between the cytoplasmic infoldings in the biopsies from the 60 to 79 year old group, but in the older group the intercellular spaces were narrower and the cell membranes tended to be straighter and to be more parallel.

A noteworthy feature was the presence of a rod-shaped cytoplasmic organelle which for convenience will be classified as a 'tubular body'. These structures were located near the cell membrane. They were dilated at each end and were membrane-bound, and the central core of the structure consisted of

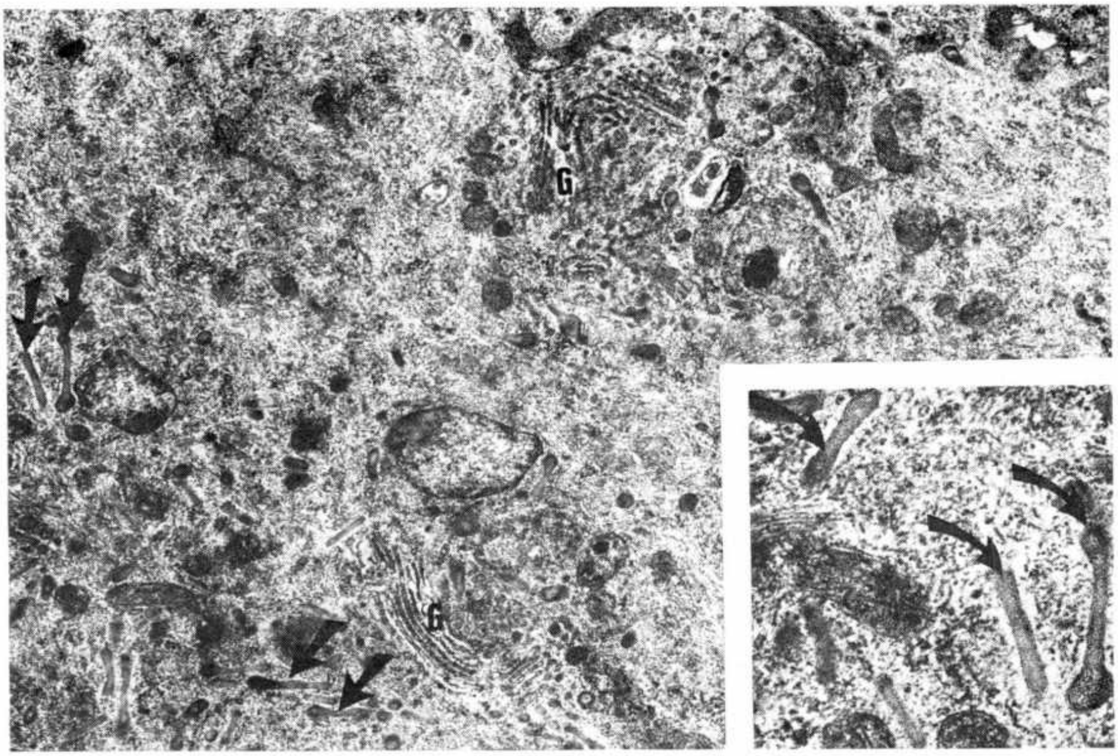

Fig. 4 *Tubular bodies are plentiful (arrows) in the cytoplasm of the intermediate cells, in which Golgi apparatus (G) is also prominent (× 22 000). The insert shows details of the tubular bodies*

electron-dense granular material (Fig. 4). The incidence of lipid vacuoles, multivesicular bodies, and myelin figures was not apparently dependent on age.

Superficial cells
It was in the cells of this layer that variation with age was the most prominent feature. In the tissue from persons aged 50 to 79 the superficial cells were polygonal and their structural components were similar to those of the intermediate cell layers. In approximately one-third of the biopsies from persons older than 80 the shape of the superficial cells became flatter and more elongated. An associated feature was the narrowing of the intercellular spaces and a reduction in frequency, height, and width of the microplicae (Fig. 5*b*). The organelle content of these 'stratified' superficial cells did not alter significantly.

In some biopsies round electron-dense structures similar to those described by Takakusaki (1969) were found in the peripheral cytoplasm. When present they were found in all the epithelial cells other than the basal layer (Fig. 5).

Goblet cells
The morphology of the goblet cells in this group of biopsies was identical to that previously described (Freeman, 1962, 1964). The cells were located in the superficial and intermediate cell layers, and their shape depended on their stage of secretion. In the mature stage the cell cytoplasm literally assumed the shape of a 'goblet' with displacement of the nucleus to the base of the cell, and the central region of the cell was filled with secretory granules (Fig. 6). The secretory granules were generally ovoid in shape and were surrounded by a membrane. Their substance was formed from alternating lamellae of electron-dense granular material, but the size and shape of the granules depended to some extent on the stage of the secretory cycle. In the early stage the secretory granules were smaller and more circular than in the mature stage, in which they were compressed.

Hyaline bodies
These amorphous structures, which were observed in the superficial layers of the epithelium by light microscopy, were studied in all 4 specimens by the

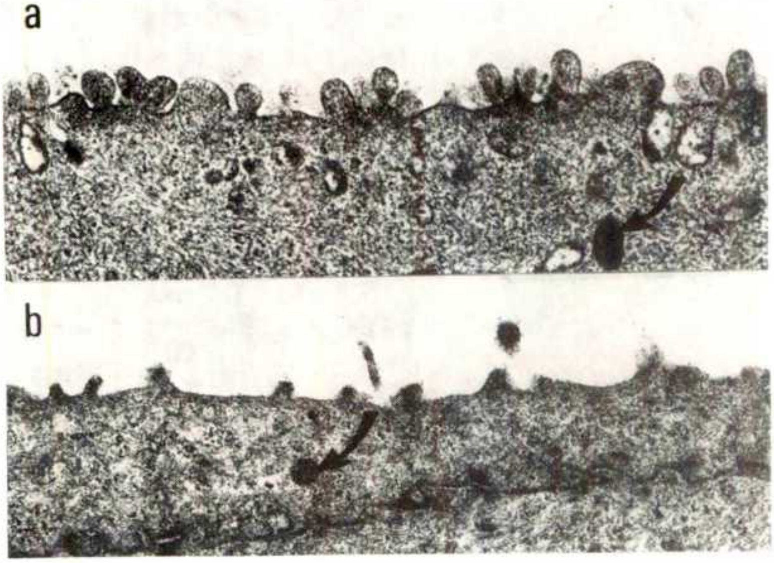

Fig. 5 *To show the comparison between (a) the surface of a normal cuboidal superficial cell with normal microplicae and (b) the surface of a superficial elongated cell in which the microplicae are stunted and reduced in number. Electron-dense structures are shown by an arrow. (a) ×26 000; (b) ×15 000*

transmission electron microscope. These 'hyaline bodies' were 2 to 3 times the size of goblet cells and were constantly circular or oval in shape. They consisted of a central, or sometimes an eccentric, electron-dense granular mass which was surrounded by a lucent zone, and this contained smaller electron-dense particles (Fig. 7). At the periphery of this electron-lucent zone there was an electron-dense rim which had an interrupted trilaminar membrane on its inner surface. The structure of this rim was found to consist of cytoplasmic tonofibrils, ribosomes, and degenerated cytoplasmic organelles. At the periphery of the central granular mass and in the lucent zone there were groups of parallel membrane-like structures interposed between granular material and small round membrane-bound circular structures of varying size. The complete 'hyaline body' was surrounded by a cell membrane bearing normal desmosome attachments.

Discussion

A previous study of tear secretion in geriatric in-patients aged over 80 indicated that 16% suffered from mild keratoconjunctivitis sicca (KCS). None of these patients had rheumatoid arthritis or proved connective tissue disease, which suggests that reduction in tear fluid was a phenomenon of increasing age (Whaley *et al.*, 1972). The clinical criteria for defining KCS are imprecise, particularly with reference to the Schirmer's tear tests and the degree of staining with Rose Bengal dye.

It is the contention of one of us (J. W.) that the dry eye syndrome is underdiagnosed, and it is possible that more precise information, for example, could be obtained from a conjunctival biopsy.

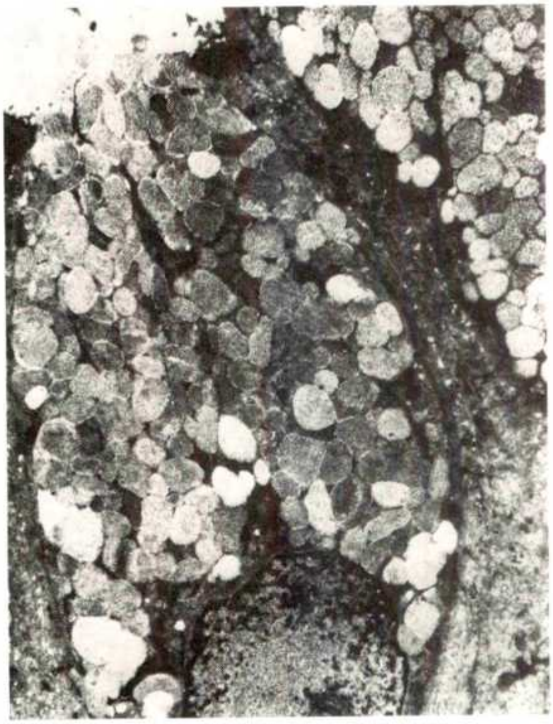

Fig. 6 *A mature goblet cell filled with secretory granules (×5000)*

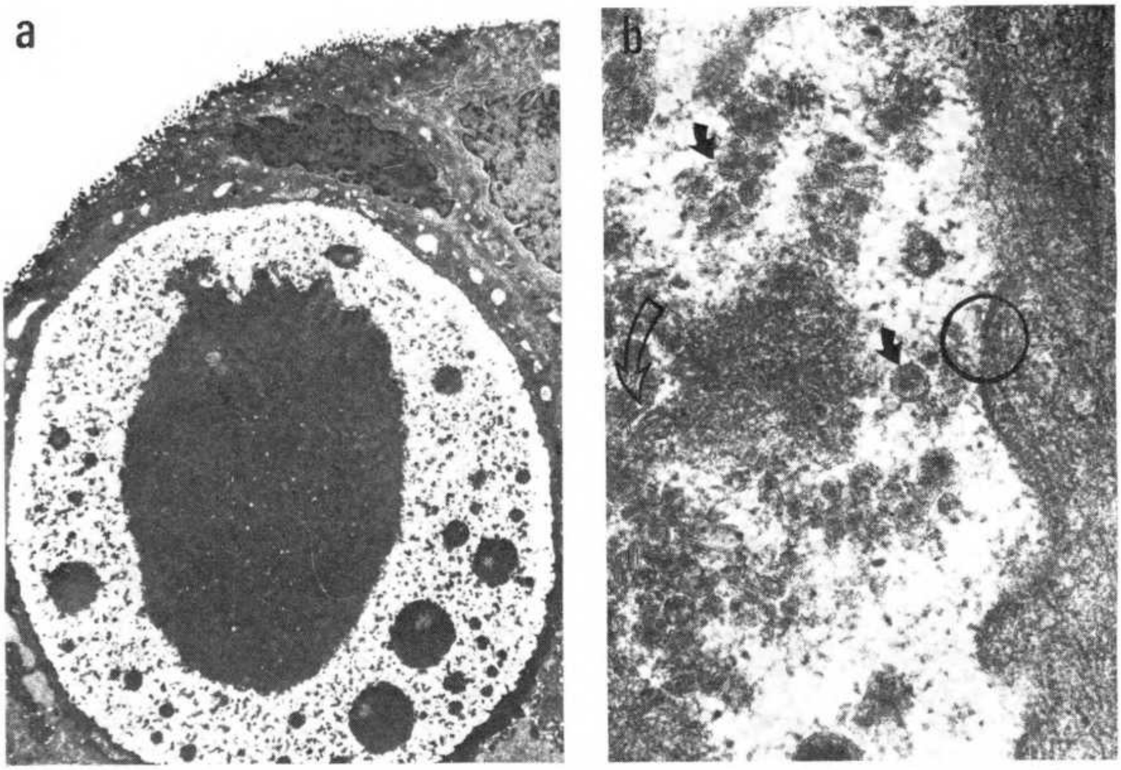

Fig. 7 *A 'hyaline body' in the conjunctival epithelium. (a) is a low power to show the electron-dense core and the surrounding lucent zone (× 3800); (b) is a higher power to show the parallel membrane-like structures (open arrow) interposed between granular material and smaller membrane-bound circular structures (fine arrows). The electron-lucent zone is limited by electron-dense material bounded internally by a trilaminar membrane (circle) (× 90 000)*

However, this presents difficulties because: (1) There is regional variation in conjunctival morphology, and (2) there does not appear to be any documentation of age change in the normal conjunctiva. Furthermore, only a few reports on the fine structure of the conjunctiva are available (Suzuki, 1956, 1957; Shibuya, 1958; Fujiyama, 1961), and these deal with relatively few specimens which were taken from the upper fornix. In the reports of Wanko *et al.* (1964) and Takakusaki (1969) on the perilimbal and palpebral conjunctiva respectively, only 6 and 4 normal conjunctival biopsies were studied, and this was insufficient to document age changes.

In the present investigation it was apparent from light and electron microscopy that significant morphological changes were rare before the age of 79 years. Segmental flattening of the epithelial cells was, however, seen in some 30% of biopsies from the group over 80 and much less frequently in the younger age groups. A constantly related feature in these patients was a lowered goblet cell count. It would appear that there was a common factor in this relationship and that there could have been a direct influence of the epithelial cells on the goblet cells. On the other hand both types of cells could have reacted to a change in their environment, as, for example, to reduced tear quantity or quality.

Alteration in the anterior surface of the elongated cells of the epithelium consisted of a reduction (size and number) of microplicae and in the incidence of the micropinocytotic vesicles. The changes in microplicae could be the result of attenuation of the cell membrane, the significant effect of which would be a disturbance in stability of the tear film. Furthermore, as micropinocytosis is thought to be a process by which macromolecules are transported into a cell, an instability of the tear film could be responsible for the lowered prevalence of micropinocytotic vesicles.

The epithelial cells did not show changes which could be associated with non-specific ageing degeneration. For example, lipofuscin granules, autophagosomes, and myelin figures were not constant or significant features in the epithelial cells from the group aged over 79.

In addition in the group aged 80 and over, if the trends are valid, the results suggest that there is a quantitative decline in the goblet cell population. The normal goblet cell population is approximately 10/mm, the proportion depending on the site studied, the highest concentration being in the lower nasal bulbar conjunctiva (Kessing, 1966, 1968; Ralph, 1975). In this series of 49 patients the goblet cell count of 9 to 10 (SD±4) confirms the above findings. However, in the group aged 80 years and above the count dropped significantly to 6±3. It is important to note, however, that neither the light nor the transmission electron microscopic studies showed any significant changes in the goblet cell morphology in any of these groups. This observation does not exclude the possibility that the basic chemical constituents of goblet cell mucosubstances were altered in a significant manner, but this is an interesting possibility and a histochemical analysis of this material is in progress.

Kessing (1968) has described alterations in the goblet cell structure and content in up to 50% of his series of patients. His contention was that the goblet cells of older people contained a high proportion of neutral mucopolysaccharides, unlike the goblet cells of younger people, in which the mucopolysaccharides were acidic. In addition, he observed frequent occlusion of the goblet cells with retention of their contents, a phenomenon which was reported to increase with age. Thus, Kessing felt that 50% of the goblet cells in elderly patients were abnormal.

In the present series, although we have been unable to confirm Kessing's findings, we have demonstrated the presence of 'hyaline bodies' in 25% of persons aged 80 and over. These, like the goblet cells, were PAS-positive and were usually associated with a low goblet cell count, suggesting a relationship between these 'hyaline bodies' and the goblet cells. In addition, if this concept holds true, that is, if the 'hyaline bodies' are due to intracytoplasmic degeneration within the goblet cells, the small membrane-like structures and the circular bodies which were seen by the transmission electron microscopy could be representative of broken down secretory granules, and the size relationships of their trilaminar membranes favours this. But since no transitional forms between goblet cells and hyaline bodies were seen in the present study the possibility of these 'hyaline bodies' being a degenerative form of goblet cells is still speculative. It has to be admitted, however, that 'hyaline bodies' were observed in only 4 of the 16 specimens examined, and the technique of transmission electron microscopy allows the examination of only small samples of tissue.

A converse situation occurred with regard to the tubular bodies (Fig. 4), which were a common feature in the intermediate cell layer. Structures similar to these bodies are a well established feature of endothelial cells throughout the vascular system (Weibel and Palade, 1964; Matsuda and Sugiura, 1970), and they were considered to be derived from the Golgi apparatus. Their function is unknown, but there has been a suggestion that in the endothelium these structures are involved in coagulation.

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References

Freeman, J. A. (1962). Fine structure of the goblet cell mucous secretory process. *Anatomical Record*, **144**, 341–345.

Freeman, J. A. (1964). Goblet cell fine structure. *Anatomical Record*, **154**, 121–147.

Fujiyama, H. (1961). Electron microscopic studies on the conjunctiva, sclera, cornea and lens crystalline. *Acta Societatis Ophthalmologicae Japonicae*, **65**, 2101–2125.

Kessing, S. V. (1966). Investigations of the conjunctival mucin. Quantitative studies of the goblet cells of the conjunctiva. *Acta Ophthalmologica*, **44**, 439–453.

Kessing, S. V. (1968). Mucous gland system of the conjunctiva. A quantitative normal anatomic study. *Acta Ophthalmologica*, Suppl. 95.

Matsuda, H., and Sugiura, S. (1970). Ultrastructure of 'tubular body' in the endothelial cells of ocular blood vessels. *Investigative Ophthalmology*, **12**, 919–925.

Ralph, R. A. (1975). Conjunctival goblet cell density in the normal subjects and in dry eye syndrome. *Investigative Ophthalmology*, **14**, 299–302.

Shibuya, Y. (1958). Electron microscopy by ultrathin specimens of normal human conjunctiva. Report I. Conjunctiva of the fornix. *Acta Societatis Ophthalmologicae Japonicae*, **62**, 1204–1213.

Suzuki, A. (1956). Fine structure of normal human conjunctiva. Electron miscroscopy in ultrathin section. *Acta Societatis Ophthalmologicae Japonicae*, **60**, 441–459.

Suzuki, A. (1957). Fine structure of normal human conjunctiva as revealed by electron microscopy in sections. *Acta Societatis Ophthalmologicae Japonicae*, **61**, 2254–2258.

Takakusaki, I. (1969). Fine structure of the human palpebral conjunctiva with special reference to the pathological changes in vernal conjunctivitis. *Achirum Histologicum Japonicum*, **30**, 247–282.

Wanko, T., Lloyd, B. J., and Mathews, J. (1964). The fine structure of human conjunctiva in perilimbal zone. *Investigative Ophthalmology*, **3**, 285–301.

Weibel, E. R., and Palade, G. E. (1964). New cytoplasmic components in arterial endothelia. *Journal of Cell Biology*, **23**, 101–112.

Whaley, K., Williamson, J., Wilson, T., McGavin, D. D. M., Hughes, G. R. V., Hughes, H., Schmulian, L. R., MacSween, R. N. M., and Buchanan, W. W. (1972). Sjögren's syndrome and autoimmunity in a geriatric population. *Age and Aging*, **1**, 197–205.

Wolfe, G. (1967). *Anatomy of the Eye and Orbit*, 7th edn. Lewis: London.

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Morphological changes in the human conjunctival epithelium. II. In keratoconjunctivitis sicca

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SUMMARY A clinicopathological correlation was performed on 24 patients suffering from keratoconjunctivitis sicca (KCS). Examination of conjunctival biopsies by light and transmission electron microscopy revealed stratification of the conjunctival epithelium with separation of the superficial cell layers, and this was directly proportional to the clinical severity of the disease. Counts of goblet cells were found to be inversely proportional to the degree of stratification. The goblet cells were morphologically identical to, but significantly fewer in number than, those found in normal conjunctival tissue. A reduction in epithelial cell stratification and separation and an increase in goblet cell density were closely related to nasolacrimal duct occlusion—an operation performed only in the severe examples of KCS in this series. The possible causes of 'mucous' plaques and 'filaments' are discussed in relation to these phenomena. Moreover, there is a dramatic reduction and deformation in the microplicae on the surface of the conjunctival epithelium. The significance of this was considered in relation to tear film stability.

In part I of this communication the study of the normal conjunctival epithelium revealed flattening of the superficial cells and a reduction in the goblet cell density in a significant proportion of the people over the age of 79 years. These appearances were observed in very few of the younger age groups. Although it was known that the incidence of mild keratoconjunctivitis sicca (KCS) rises with age (Whaley *et al.*, 1972), it was impracticable to examine all the individuals in this 'normal' control group for the presence of a dry eye. It is possible, therefore, that some of the normal group were suffering from a mild, clinically undetected form of KCS.

This background information was necessary for the purpose of the present study, in which the morphology of the conjunctival epithelium was examined in patients suffering from definite KCS in both rheumatoid arthritis (Sjögren's syndrome) and in the sicca syndrome. An attempt has been made to reassess the observations made on the normal tissue, to establish the pathological changes which might be specific for KCS, and to assess the effect of current therapy on the epithelial morphology in KCS.

Materials and methods

Conjunctival biopsies were obtained by the surgical technique which was described in part I except that retrobulbar anaesthesia was not required. Thirty patients volunteered for this study, and the details of age, sex, clinical severity, duration, and relevant therapy are shown in Table 1. The site of biopsy was the same as that for the procedure described in part I and the methods for fixation and tissue distribution for qualitative and quantitative light microscopy and qualitative electron microscopy were identical to those previous employed. After morphological assessment 6 specimens were excluded from the group because the technical quality of the material was inadequate.

Results

From Table 1 it can be seen that the average age (±SD) of the patients, 22 of whom were female and only 2 male, was 61 ± 13. Eight patients had the sicca syndrome, there was 1 case of Still's disease, and the remaining 15 suffered from Sjögren's syndrome.

The clinical duration of the disease in both rheumatoid arthritis and KCS varied considerably, and this was unavoidable because the patients were selected on the basis of availability and willingness to co-operate in the study.

LIGHT MICROSCOPY

The material was examined without prior knowledge of the patients' clinical status and the following

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Table 1 *Summary of clinical status, and morphological findings in a series of KCS patients*

Case No.	*Age*	*Duration (years)*			*Treatment*	*Degree stratification*	*Goblet cell count/mm*	*Comment*
		RA	*Sicca*	*KCS*				
1	66		4	3	O (2), T, M	0	8	Well controlled
2	62	12		8	O (4), T	0	11·2	Well controlled
3	50	39		10	T	0	6·6	Mild
4	74	6		3	T	0	8·5	Mild
5	71	20		14	T, M	0	8	Moderate
6	51	2		3	O (2), T	0	8·7	Well controlled
7	73		12	10	O (5), T, M	0	10·6	Symblepharon
8	27	4		1	—	0	8	Mild
9	69	10		8	O (2), T	1	8·3	Well controlled
10	44	26		3	T	1	6·6	Mild
11	53		5	5	Betnezol	1	1·7	+ episcleritis
12	69	20		6	T, M	1	5·4	Moderate
13	70	10		6	O (2), T	2	2·3	Difficult control
14	61		>1	>1	T	2	2·6	Severe
15	72		4	4	—	2	0	Severe
16	68	(Still's disease)		1	—	2	0·5	Severe, new case
17	78		8	4	T	2	0	Severe
18	67	10		3	T	2	0·7	Severe
19	41	>1		>1	—	2	0	Severe, new case
20	40		11	8	T, M	2	0·6	Severe
21	65	12		2	T	2	0	Mild
22	74	15		1	T	2	0·3	+ blepharitis
23	64		1	1	—	2	2·4	Severe, new case
24	56	12		>1	—	2	0·5	Severe, new case

O = duct occlusion. T = tear substitute. M = mucolytic agent. The numbers in parentheses indicate the period (years) between duct occlusion and biopsy

morphological changes were found to be of relevance.

Epithelial stratification

Stratification of the epithelium (Fig. 1) was a feature common to almost every biopsy examined. In severity, however, it varied and was classified into 3 grades. Grade 0: The mildest form in which there was evidence of superficial segmental flattening and elongation in about 25% of the total length of the epithelium available for study, but this was of insufficient severity to make it readily distinguishable from the normal. Grade 1: Approximately 25 to 50% of the total length of the epithelium showed stratification. Grade 2: At least 50 to 75% or more of the total length of the epithelium showed stratification.

Eight patients were classified as grade 0, 4 as grade 1, and 12 as grade 2. This assessment was repeated on coded sections some 6 months after the first assessment and the results were essentially similar.

Reduction in goblet cell density

The goblet cell population was found to be reduced in nearly every case. In those specimens which showed grade 0 stratification the mean count (±SD) was 8±2, which was near to the normal level of 10±3 cells/mm. On the other hand in the specimens which showed grade 2 stratification, the goblet

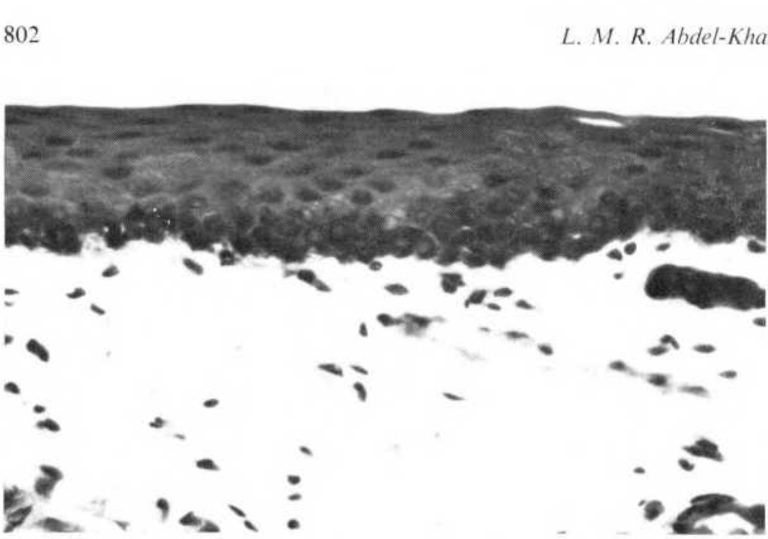

Fig. 1 *A light micrograph to show an example of superficial and intermediate cell flattening, or 'stratification', of moderate degree. H and E (× 375)*

cells were significantly reduced to a mean ± SD of 0·8 ± 1·0. Indeed in 4 of the 12 specimens with severe stratification there were no goblet cells in the epithelium. There appeared to be no relationship between the age of the patient, the duration of arthritis or KCS, and the conjunctival pathology and goblet cell population in this series. Moreover, with a few exceptions, those graded clinically as mild or well controlled showed little stratification, and the goblet cell counts approached the normal. The most significant observation was that those patients who were treated by nasolacrimal duct obliteration and whose treatment was considered to be satisfactory for periods varying between 2 and 5 years had few abnormal features in the morphology of the conjunctival biopsies (Table 1).

Inflammatory cells, lymphocytes, plasma cells, and polymorphonuclear leucocytes were identified in the stroma and epithelium, but the distribution and number were variable and no significant patterns emerged.

ELECTRON MICROSCOPY

The most marked changes in the ultrastructure of the epithelium were seen in the untreated cases of KCS in Sjögren's syndrome and in the sicca syndrome; no morphological distinctions could be made between these 2 groups of patients. The alteration in epithelial cell morphology was simply one of a change in shape, and apart from separation of the superficial cells the organelle content and the nuclear chromatin pattern remained essentially the same throughout the epithelial layers. The disordered orientation of the epithelial cells extended frequently to the intermediate cells, and in the most advanced examples of stratification the basal cell layer was involved (Fig. 2). In all cases, however, the intercellular relationships between the elongated intermediate and basal cell layers were preserved, and the interdigitations and intercellular junctions were apparently normal. Nevertheless, the slight widening of the intercellular spaces, which is a feature of the normal intermediate cell layer, was less prominent in the diseased epithelium.

The principal feature of interest was a widening of the intercellular spaces between the superficial and the subjacent cells. This process of superficial cell separation was found to vary with the severity of stratification. In the mildest form no marked separation could be seen. At a later stage the intercellular space was widened and processes extended from the cells into the intercellular space, which contained fine electron-dense strands (Fig. 3). Often the underlying cells were relatively more electron - dense and contained intracytoplasmic vacuoles, which suggested involvement of this cell layer in the pathological process. The separating superficial cells contained membrane-bound structures; the rough endoplasmic reticulum showed focal dilatation and the cytoplasm was of diminished density. The microplicae were reduced in number and height. However, the anterior cell membrane was usually intact.

In the more advanced stages of separation the cytoplasm of the separating cells was electron-lucent and the organelle content was markedly diminished. Occasionally membrane-bound vesicular structures were present in the cytoplasm and the nuclear membrane was disrupted with loss of nuclear chromatin into the cytoplasm. The processes from the detaching cells were contracted, and the cytoplasm within them was electron-lucent. The anterior surface showed marked or total loss of microplicae with, in addition, disruption of the anterior cell membrane (Fig. 4). By contrast the intercellular apical junctions were preserved and the attachments

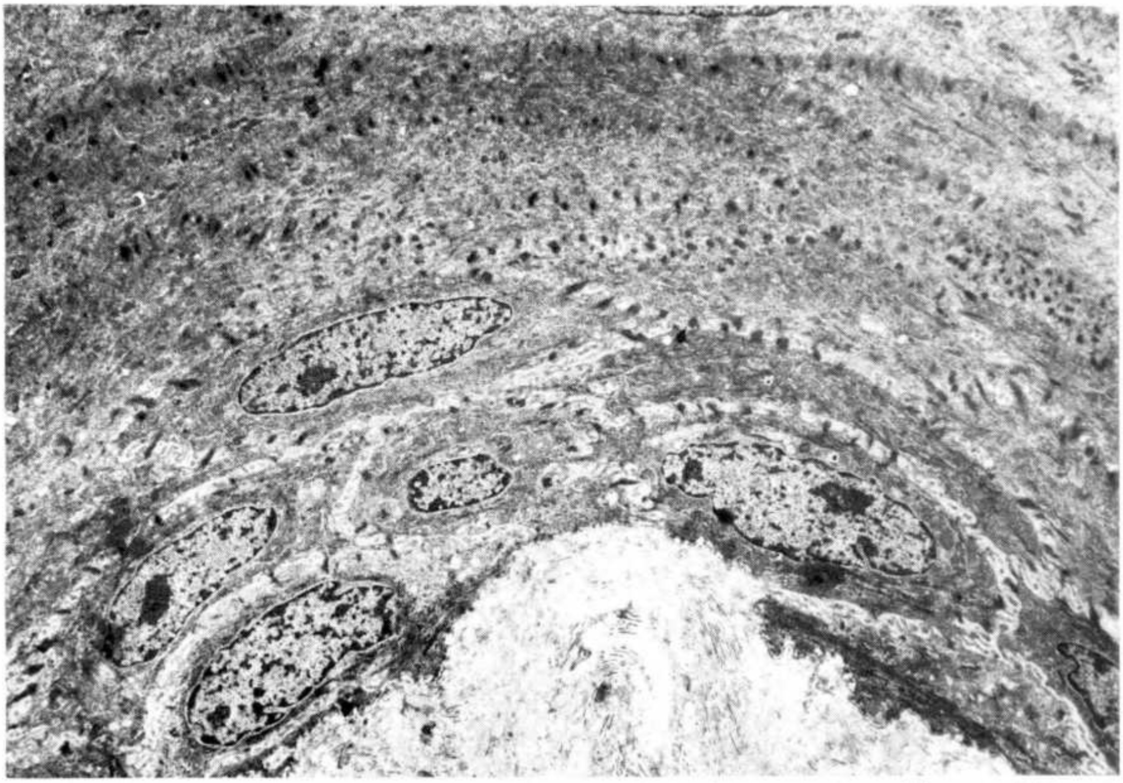

Fig. 2 *An electron micrograph to show advanced stratification on the basal and intermediate cell layers* (× 3800)

between the cells of the superficial layer persisted, so that elongated strips of cells were detached from the subjacent layer.

In all grades of involvement the morphology of the goblet cells was identical to that described in the control group. Hyaline bodies were not observed in any of the biopsies in the KCS series.

Discussion

The most important feature in this investigation was the almost constant finding of stratification in the epithelium of patients suffering from KCS. Whether this is the result of reduced lacrimal secretion in part or whole is a matter for speculation. In this study the most severe forms of stratification were to be found in those patients classified clinically as severe forms of KCS. Furthermore, an apparent reduction in stratification and an improvement in the goblet cell count was closely related to nasolacrimal duct occlusion. Although the numbers in the series are few, this observation was consistent, and its significance is enhanced when it is noted that only severe examples of KCS were treated by this operation. Thus, if the improvement in the tear coverage following the occlusion procedure was unrelated to the observed conjunctival changes, it would be necessary to find another causal relationship. At present it would appear that nasolacrimal duct occlusion is the only common feature to this improvement in epithelial morphology.

A reduced goblet cell population is a known feature in patients suffering from dry eye (Ralph, 1975). In the region of conjunctiva examined in this study the goblet cell count was inversely proportional to the degree of stratification. Moreover, these goblet cells were morphologically identical to those described in the normal tissue in part I. In view of this observation it is of interest to speculate on the possible cause of the accumulation of mucus in severe cases of KCS. If the samples used for this investigation are to be regarded as representative, it must be assumed that there is a reduction in the total goblet cell count throughout the conjunctiva, although it must be conceded that the assumption may not be entirely valid (Kessing, 1966).

However, if the assumption is accepted, there are 2 possible explanations for the accumulation of

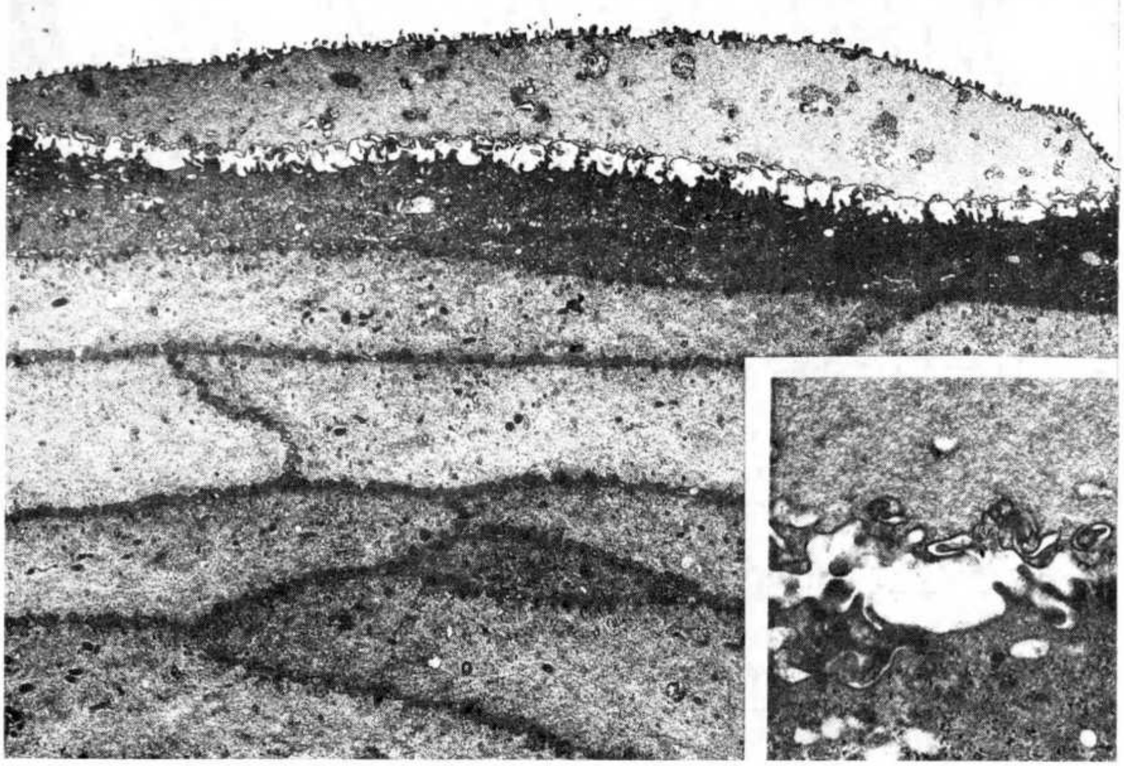

Fig. 3 *An example of stratification in which there is separation of the superficial layer. The insert shows the stunting of the cell processes in the intercellular space* (× 3400; insert × 14 000)

mucus. Firstly, normal mucus could accumulate because there is inadequate wash-through by normal tear secretion. Secondly, there could be an alteration in the relative proportions of the 5 glycoproteins which are secreted by the goblet cells and this could change the physical and/or biochemical properties of the tear film (Wright, 1974).

Careful examination of the conjunctiva in KCS will frequently reveal the existence of tiny filaments, the cause and nature of which are controversial. This investigation suggests that the separation of sheets of superficial cells may contribute to these filaments. On the other hand reduction in the number of filaments frequently follows on treatment with mucolytic agents (Jones and Cook, 1965; Williamson *et al.*, 1974), and it may be argued that filaments are therefore mucous threads which are attached to separating epithelial cells. Recent studies of 'mucous' plaques from the corneal surface in patients which KCS have shown these to consist of a mixture of mucus and desiccated epithelial cells (Fraunfelder *et al.*, 1977). In the present study the epithelial cells showed a tendency to separate in sheets, and, since the intercellular junctions between these cells were preserved, it can be assumed that these changes are not entirely a degenerative phenomenon.

It is also possible that the separation of sheets of superficial cells is a mechanical process caused by the eyelids rubbing over the relatively dry surface of the bulbar conjunctival epithelium. Thus a shearing effect might account for the withdrawal of cytoplasmic processes from the intercellular space (see Fig. 4). Another feature of major importance in relation to the surface morphology is the dramatic reduction and deformation seen in the microplicae. Under these circumstances even in the presence of a normal tear secretion it would seem unlikely that a tear film could be maintained.

The increase in stratification of the conjunctival epithelium in association with the severity of the

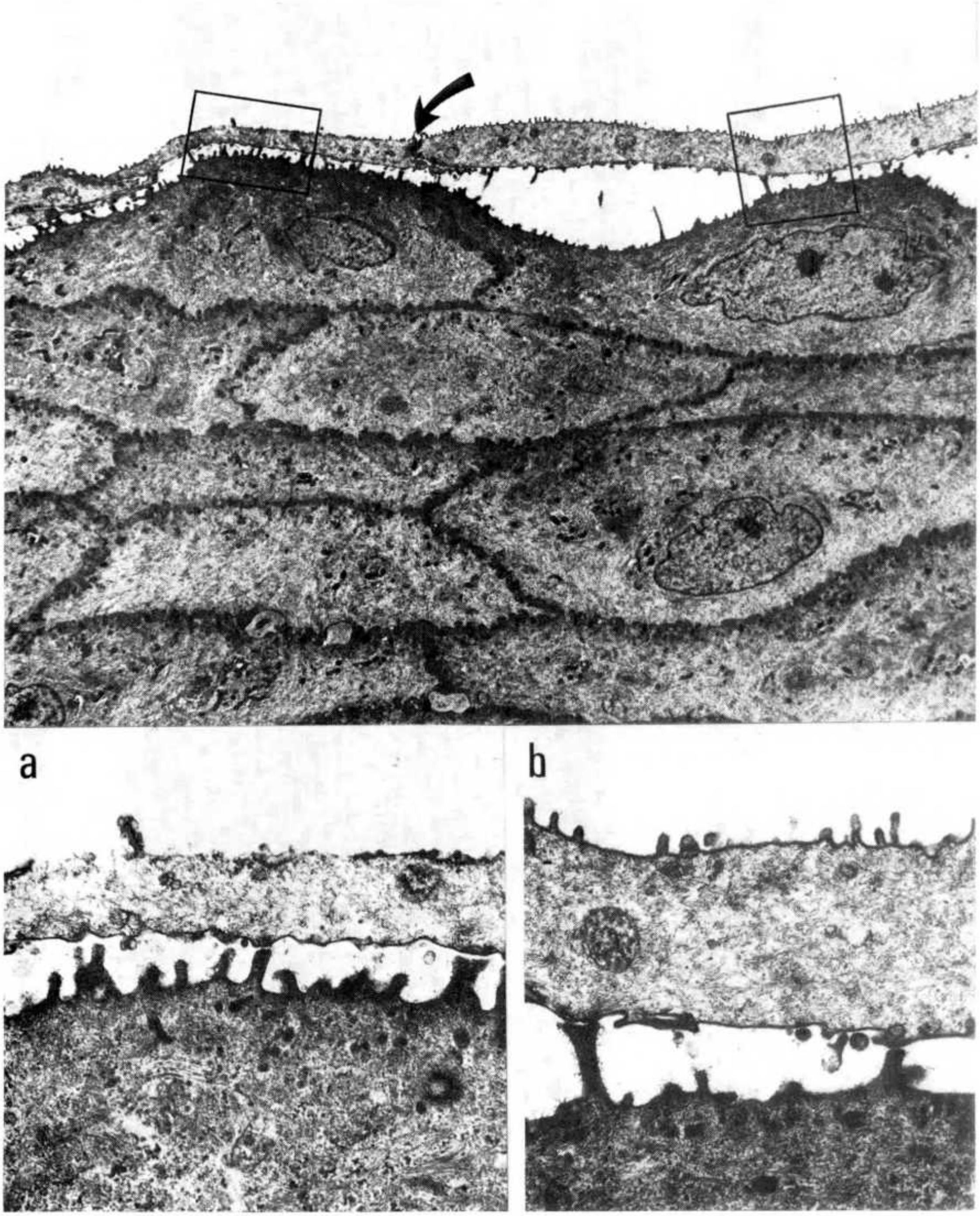

Fig. 4 *An example of a more advanced separation of the superficial cell layer. Note the presence of the apical junction (arrow) and the severe loss of microplicae. The insert (a) shows disruption of the anterior cell membrane and (b) shows advanced stunting of the cell processes* (× 3350; inserts × 17 500)

KCS suggests that it is a protective mechanism evolved by the change in the tear secretion, but it may also be an intrinsic and basic response of the cells to a hostile environment. Whether or not the cell stratification is a cause or a result of the diminished goblet cell density remains a subject for further investigation.

Another well documented condition in which epithelial stratification has been observed in association with goblet cell depletion is severe vitamin A deficiency, a condition which is reversible with systemic vitamin A therapy (Sullivan *et al.*, 1973). Vitamin A has been used in the past as a treatment for KCS, but the results were disappointing and the pathogenic mechanisms for this ultimate morphological response are probably unrelated. Nevertheless in this study we have observed a tendency to return to morphological normality in the conjunctiva of patients treated for 2 to 5 years previously by nasolacrimal duct occlusion. The stratification and superficial cell separation was less and the goblet cell count was higher than in untreated patients with KCS, and this return to near normality was associated with clinical improvement of these patients. It should be remembered at this point that the patients selected for obliteration of tear passages were all examples of severe KCS judged to be inadequately controlled by at least 1 year of tear substitute therapy (Williamson *et al.*, 1974).

This research was conducted under the auspices of the W. H. Ross Foundation (Scotland) for the Study of the Prevention of Blindness. The authors also thank Mr R. A. Muirhead and Mr J. Ralston for technical support, and Mrs M. Olivier for secretarial assistance.

References

Fraunfelder, F. T., Wright, P., and Tripathi, R. C. (1977). Corneal mucous plaques. *American Journal of Ophthalmology*, **83**, 191–197.

Jones, B. R., and Cook, M. U. (1965). The management of keratoconjunctivitis sicca. *Transactions of the Ophthalmological Societies of the United Kingdom*, **85**, 379–390.

Kessing, S. V. (1966). Investigations of the conjunctival mucin. Quantitative studies of the goblet cells of the conjunctiva. *Acta Ophthalmological (Kbh)*, **44**, 439–453.

Ralph, R. A. (1975). Conjunctival goblet cell density in normal subjects and in dry eye syndrome. *Investigative Ophthalmology*, **14**, 299–302.

Sullivan, W. R., McCulley, J. P., and Dohlman, C. M. (1973). Return of goblet cells after vitamin A therapy in xerosis of the conjunctiva. *American Journal of Ophthalmology*, **75**, 720–725.

Whaley, K., Williamson, J., Wilan, T., McGavib, D. D., Hughes, G. R. V., Hugh, M., Schmulion, W. R., McSween, R. N. M., and Buchanan, W. W. (1972). Sjögren's syndrome and autoimmunity in a geriatric population. *Age and Ageing*, **1**, 197–202.

Williamson, J., Doig, M. W., Forrester, J. V., and Thain, W. C. (1974). The management of the dry eye in Sjögren's syndrome. *British Journal of Ophthalmology*, **58**, 798–805.

Wright, P. (1974). Sjögren's syndrome. *Transactions of the Ophthalmological Societies of the United Kingdom*, **94**, 764–772.

Book reviews

Atlas of the Human Brain and the Orbit for Computed Tomography. By JOSEPH HANAWAY, WILLIAM R. SCOTT, and CHARLES M. STROTHER. 1977. Pp. 76, figs., refs. Warren H. Green, St. Louis, Missouri ($22·50)

After an introduction of 2 pages a series of photographs follows showing sections of the brain with the corresponding computed tomography (CT) scan. Three planes are studied—the horizontal, 25° from the horizontal plane, and 35° from the horizontal plane. The anatomical slices are well labelled and the orbital sections adequate. Unfortunately, technological advances have meant that the CT scan pictures are now outdated, and the additional dimensions obtained by coronal and sagittal scanning are also omitted. This book, though printed in 1977, is already out of date, and an updated version would seem necessary to provide an adequate atlas. M. D. SANDERS

Glaucoma Symposium, Würzburg 1974. Edited by W. LEYDHECKER. 1977. Pp. 302, figs., tables, refs. Ferdinand Enke Verlage, Stuttgart (DM112)

This report on a glaucoma symposium held at Würzburg in 1974 contains 24 papers covering a wide range of topics related to glaucoma diagnosis and therapy. All contributions are in German, with English summaries.

T. J. FFYTCHE

Obituary

A. B. Nutt, LLD, MSc, MB, FRCS

Mr A. B. Nutt, formerly consultant ophthalmic surgeon to Sheffield United Hospitals, died on 27 February. He was 79.

Albert Boswell Nutt, affectionately known by everyone as Bertie, was born in Sheffield on 7 July 1898. He was educated at King Edward VII school in Sheffield and entered Sheffield University to read physiology and medicine. His studies were interrupted by service in the eastern Mediterranean during the first world war with the Royal Naval Volunteer Reserve, but his natural aptitude for science and medicine nevertheless enabled him to graduate with first-class honours in 1923, with gold medals in both clinical medicine and surgery. He soon concentrated on his chosen subject of ophthalmology and in 1927 was appointed honorary ophthalmic surgeon to the Sheffield Royal Infirmary. It is not generally known that as long ago as 1932 he and his pathologist colleague, Cecil Paine, were the earliest successful pioneers in treating eye infection by local applications of penicillin, which had been prepared in the infirmary. He never lost interest in the wider aspects of ophthalmology and its relationship to general medicine.

His appointment in 1938 as ophthalmologist to the Sheffield Children's Hospital led to his overriding interest in ocular motility and strabismus. A pioneer in this country of modern surgical techniques in strabismus, he was a meticulous surgeon whose excellent results led to patients with difficult mobility problems being referred from a wide area. He founded the Sheffield Orthoptic School and was chairman of the British Orthoptic Board from 1958 to 1970, guiding its reorganisation into the British Orthoptic Council. He was always a great supporter of the orthoptic profession.

His work on ocular motility led to his appointment as Hunterian professor of the Royal College of Surgeons in 1954. The college granted him an honorary fellowship, and he served it as examiner, representing the Faculty of Ophthalmologists on the college council for 5 years. His wise councils were recognised by the Faculty of Ophthalmologists, which elected him president from 1963 to 1965.

He was vice-president of the Ophthalmological Society of the United Kingdom, but his greatest love was perhaps the Oxford Ophthalmological Congress, of which he was Master in 1961 and 1962. It was the enthusiasm and wisdom of Bertie and the council members of his generation that guided the Oxford Congress through a period of rapid growth to the international recognition that it enjoys today, maintaining and extending the unique atmosphere of friendship that is the hallmark of that congress. His friendships extended throughout the world, aided by travelling widely even in the days before easy intercontinental flying.

His activities were not confined to ophthalmology, for he was a member of council, court, and convocation of the University of Sheffield, being chairman of convocation from 1964 to 1967, and in 1974 his services were recognised by the grant of the degree of doctor of laws. He was a member, and eventually chairman, of the venerable charitable organisation, the Sheffield Town Trust. He was also a prominent Freemason, joining the University Lodge in his days as a student and eventually holding many offices, including Assistant Provincial Grand Master of the province of Yorkshire West Riding.

Bertie was one of the most widely loved of Sheffield citizens and was one of our leading Ophthalmologists, yet he remained essentially a kind, humane, and humble man, keeping close to nature in his large garden, which occupied much of his thoughts and his meagre spare time.

A.S.

Notes

Orthoptic congress

The Fourth International Orthoptic Congress organised by the International Orthoptic Association and the Swiss Orthoptic Association will take place in Berne, Switzerland, on 3 to 6 September 1979. Further information can be had from Ursula Altmann, Himmeriweg 8, Zurich, Switzerland.

Practical microsurgery

The 8th course of practical ocular microsurgery will be held at Nantes on 26–28 February 1979. The theme will be surgery of the vitreous. Joint presidents will be Dr Freeman of Boston, Dr R. Klotti of Zurich, and Dr J. D. Scott of Cambridge. Further information from Dr P. Sourdille, 16 boulevard G. Guist'hau, 44000 Nantes, France.

Eye research award

The winner of the annual $25 000 William and Mary Greve International Research Scholars award of Research to Prevent Blindness Inc is Daniel M. Albert, professor of ophthalmic pathology at Harvard Medical School. Scientists of all nations are invited to submit nominations for the 1979 award. It is given each year to advance the work of an outstanding young MD or PhD scientist who is exploring new concepts of saving sight. Formal nominations must be received by 1 March 1979. Heads of medical school departments of ophthalmology and interested ophthalmic scientists should request application information immediately from Research to Prevent Blindness Inc, 598 Madison Avenue, New York, NY 10022, US.

Twelfth Symposium Radiologicum

Dr Giovanni di Chiro, chief of the neuroradiology and computed tomography section of the National Institutes of Health, Bethesda, Maryland, USA, has been elected president of the XII Symposium Neuroradiologicum, which will take place in Washington, DC, on 10–16 October 1982. The vice-president is Dr Hillier L. Baker, of the Mayo Clinic, and the secretary-general is Dr David O. Davis, of the George Washington University Medical Center.

Contact lens fitting

The Rudolph Ellender Medical Foundation (an AMA-approved course in continuing medical education) will be presenting its nineteenth annual instructional course in contact lens fitting in New Orleans on 29–30 March 1979. Further details from Rudolph Ellender Medical Foundation Inc, Roof, Delta Towers, New Orleans 70112, USA.

Norman McAlister Gregg lecture

Dr Robert Ellsworth, of New York, will deliver the Norman McAlister Gregg lecture at the scientific congress of the Royal Australian College of Ophthalmologists to be held in Brisbane on 7–12 October 1981. Further information from the Executive Secretary of the College at 27 Commonwealth Street, Sydney, New South Wales 2010, Australia.

Ophthalmic microsurgery

The fourth annual New Orleans Spring Fiesta Ophthalmic Microsurgery seminar will be held on 3–5 May 1979. The subject will be cataract surgery and intraocular lens implantation. Further information from the Azar Foundation, 144 Elk Place, Suite 1501, New Orleans, Louisiana 70112, USA.

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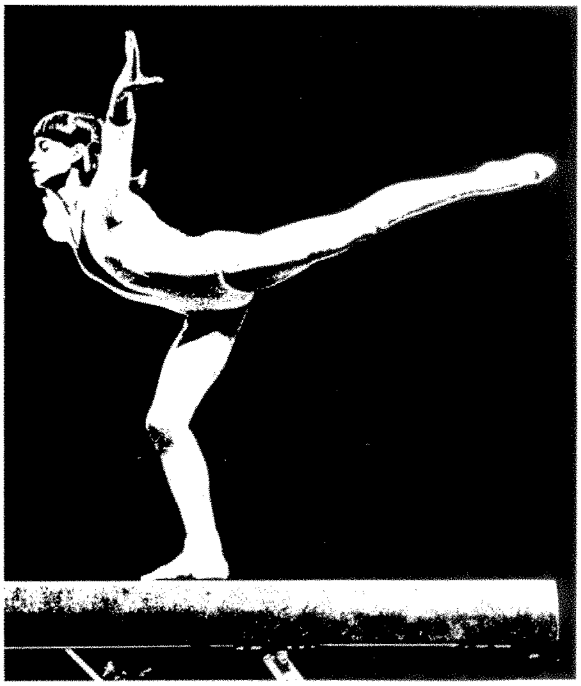

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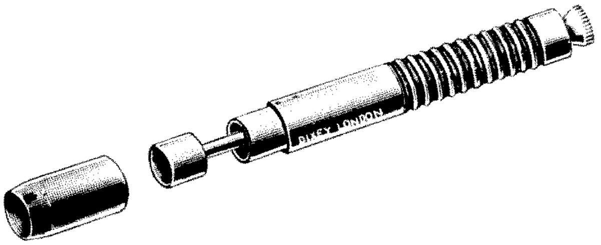

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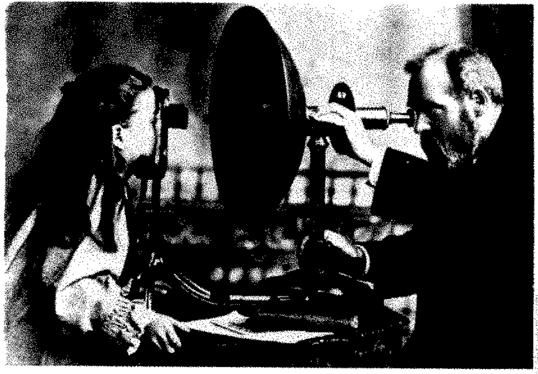

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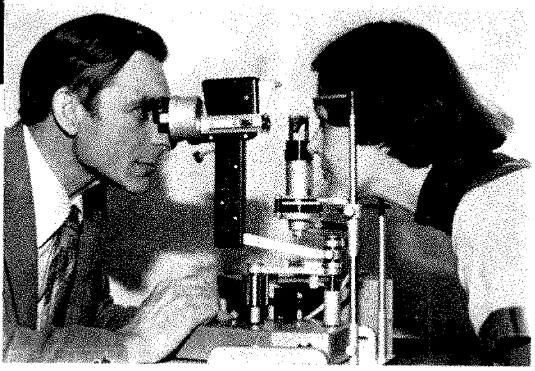

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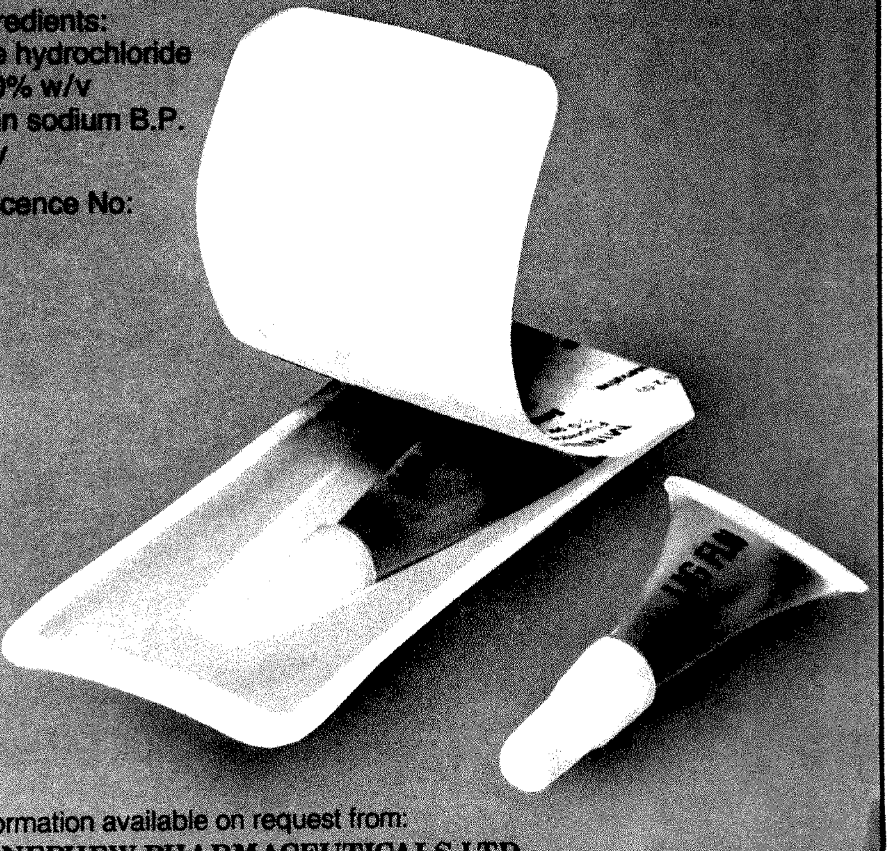

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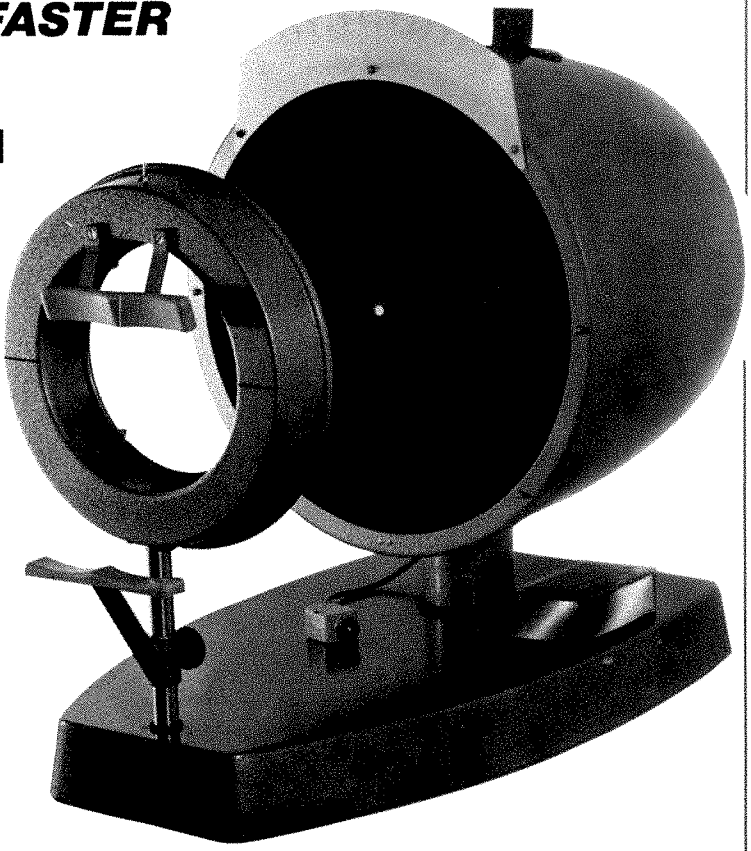

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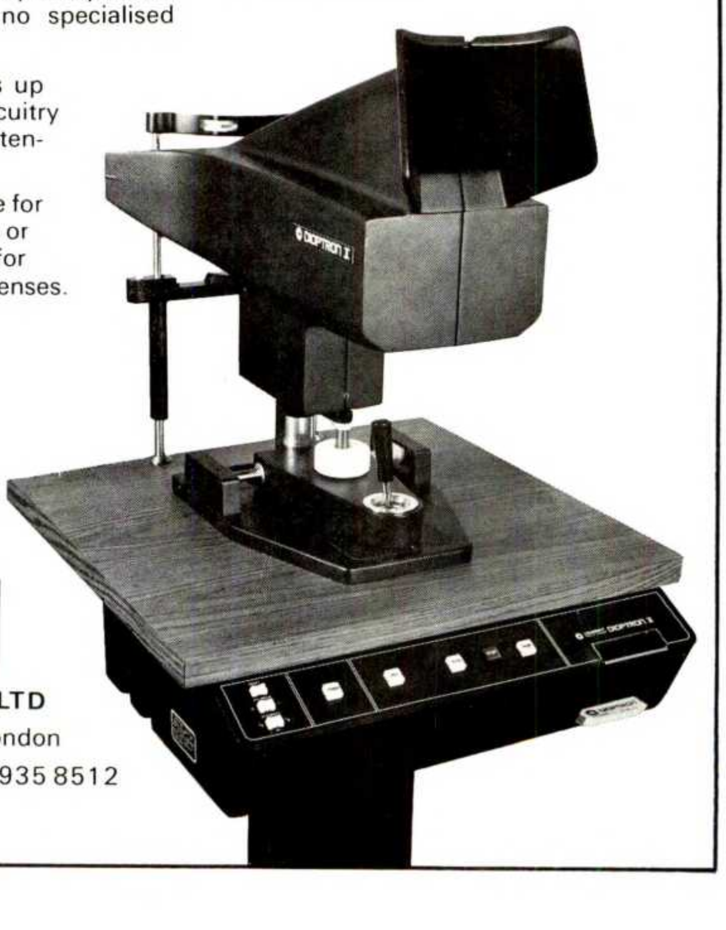

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British Journal of Ophthalmology, 1978, **62**, 809–814

Specular microscopy of the corneal endothelium

G. D. STURROCK, E. S. SHERRARD, AND N. S. C. RICE

From the Pocklington Eye Transplantation Research Unit, Institute of Ophthalmology, London, and Moorfields Eye Hospital, City Road, London

SUMMARY The endothelium of the normal corneas of 67 human subjects was studied *in vivo* with the specular microscope in order to quantify the method as a means of sampling the cell density of the tissue. It was found that (1) axial cell counts of the endothelium are reproducible in the same cornea after an interval of time; (2) the cell counts of the centre and periphery of the same cornea are similar; (3) the axial cell counts of pairs of eyes are similar; and (4) there is a gradual reduction of cell number with increasing age. The significance of these data is discussed.

Although it is possible to observe the individual cells of the corneal endothelium with the use of the biomicroscope and specular illumination (Vogt, 1919), eye movements and the limited magnification available virtually preclude the use of this technique for systematic study of the endothelium. These problems have been largely overcome by the introduction of the specular microscope (Maurice, 1968), which was subsequently adapted for clinical use by replacing the original water immersion lens with a dipping cone objective which applanates the cornea (Laing *et al.*, 1975). With this instrument it is possible to examine and photograph the corneal endothelium at high magnification *in vivo*. Several authors have published their findings with the clinical specular microscope (Laing *et al.*, 1976a, b; Bourne and Kaufman, 1976a, b, c; Bourne *et al.*, 1976), and the optical principles have been discussed (Bourne and Enoch, 1976). Recently the use of an auxiliary lens to obtain a wider field of view has been described (Sherrard, 1976).

The purpose of the present study was to quantify the method of sampling corneal endothelial cell density with the specular microscope. Endothelial cell counts were performed on 67 subjects of various ages and the following 4 parameters were investigated—the reproducibility of axial cell counts, the relationship between axial and peripheral cell counts in the same eye, the relationship between axial cell counts from pairs of eyes, and the variation in axial cell density with age.

Materials and methods

APPARATUS AND PHOTOGRAPHY

The construction of the prototype specular microscope used in this study is shown in Figs. 1 and 2. Kodak Tri-X film (ASA 400) was used for all photographs. The film contrast was increased by force-developing with Ilford Contrast FF developer, diluted 1 in 4, for 2½ minutes at 20°C, followed by normal fixing and printing. Specular photomicrographs of corneal endothelium are shown in Fig. 3.

Between 7 and 10 randomly selected areas of endothelium were photographed in the axial region of 1 or both corneas of all subjects. After an interval of some weeks 16 subjects were rephotographed. In 9 subjects the peripheral endothelium was also photographed at 2 sites, 3·5 to 4 mm from the nasal and temporal limbus respectively, in the horizontal meridian.

The pressure exerted by the objective on the subject's cornea was repeatedly checked during each photographic session. This was facilitated by the position of the viewing ocular, which projected at right-angles from the microscope, thus enabling the photographer to sit close-up beside the subject. Apart from the production of transient punctate epithelial erosions no corneal damage was caused by specular microscopy.

CALIBRATION AND CELL COUNTING

The specular microscope was calibrated by photographing a graticule mounted 0·5 mm from the dipping cone objective, the interspace being filled with saline. A photograph of the graticule was back-projected on to a screen from the same fixed distance at which the photographs of the corneal endothelium were subsequently projected. The film magnification was measured as 47·5× and the total linear magnification on the screen was found to be 358×.

Cell counting was performed by making film contact prints from the negatives and back-projecting

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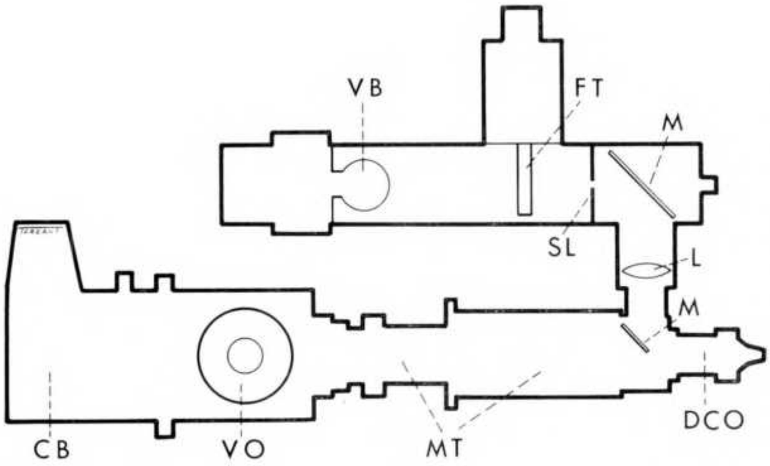

Fig. 1 *Diagram of specular microscope. VB: rheostat-controlled 15-W viewing bulb; FT: parfocal 60-W/S Xenon flash tube; SL: adjustable slit aperture; M (upper): adjustable mirror; L: 20-dioptre lens; M (lower): fixed mirror; DCO: Nikon × 20 dipping cone objective; MT: microscope tube; VO: viewing ocular (projecting at right-angles); CB: camera body*

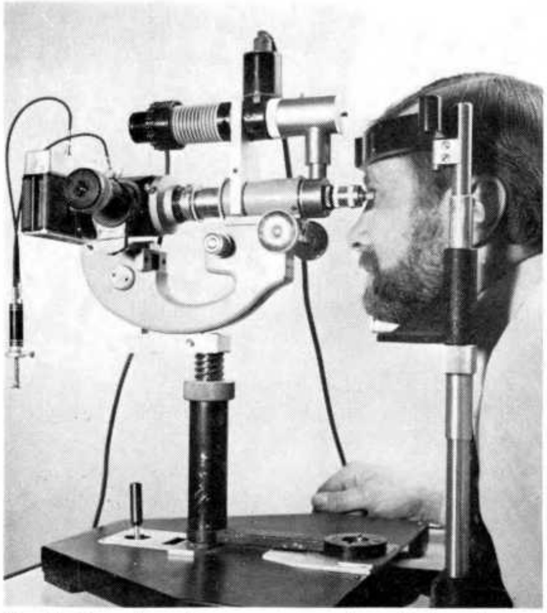

Fig. 2 *Specular microscope mounted on slit lamp base and aligned with subject's left cornea*

them on to the screen at the linear magnification of 358× established above. A rectangle of known area was placed on the screen, and the number of cells enclosed by the rectangle was counted. Cells touching the left-hand side and top of the rectangle were excluded, while cells touching the right-hand side and bottom were included in the count. Four different sizes of rectangle were available because the area of cells which could be counted was variable owing to the presence of hazy areas or dark folds on some photographs. The largest rectangle was used wherever possible to include the greatest number of cells. In order to reduce counting errors a clear celluloid sheet was placed over the counting rectangle, and each cell was marked with an ink dot as it was counted. The number of cells counted per photograph varied between 40 and 100.

Owing to regional variations in endothelial cell density the 7 to 10 photographs taken per cornea recorded a range of cell counts from which the mean cell count for each cornea was calculated.

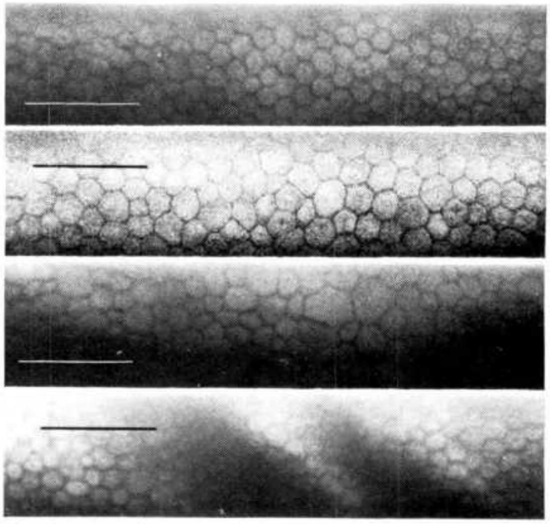

Fig. 3 *Specular endothelial photographs. (a) Small uniform cells. Density 3100 cells/mm^2. Female 13 years. (b) Larger cells, fairly regular in size. Density 1980 cells/mm^2. Female 76 years. (c) Marked variation in cell size. Density 2080 cells/mm^2. Female 61 years. (d) Dark posterior corneal wrinkles due to dipping cone objective. Density 2900 cells/mm^2. Male 62 years. Bar = 100 μm*

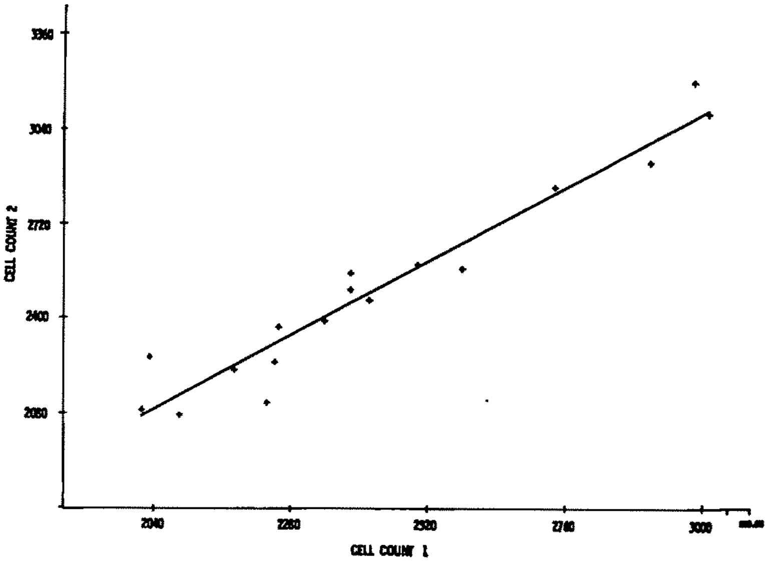

Fig. 4 *Original mean cell count (cell count 1) plotted against repeat count (cell count 2) from 16 eyes to demonstrate reproducibility of counting technique*

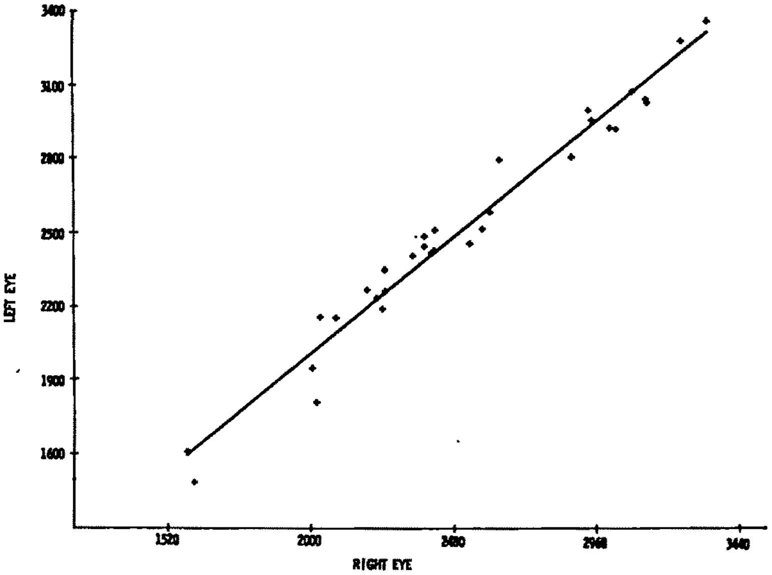

Fig. 5 *Mean cell counts from right and left eyes of 31 patients plotted against each other to show close agreement between the 2 eyes of each patient*

SUBJECTS

The endothelial cell counts presented here were obtained from hospital patients, the majority of whom were awaiting surgery for squint, obstructed lacrimal drainage, retinal detachment, or cataract. One of both eyes of each subject were included if prior biomicroscopic examination revealed a healthy clean cornea without endothelial guttae and no signs of inflammation, past or present, in the anterior segment. Eyes with a history of blunt or penetrating trauma, previous surgery, uveitis, or glaucoma were excluded. Eyes with uncomplicated senile lens opacities were included in the study.

Results

REPRODUCIBILITY

Axial endothelial cell counts were performed on 1 eye each of 16 subjects (8 males, 8 females, aged 48 to 52 years), and after an interval of 3½ to 20 weeks (average 7 weeks) the same eyes were rephotographed and the cells recounted. A comparison

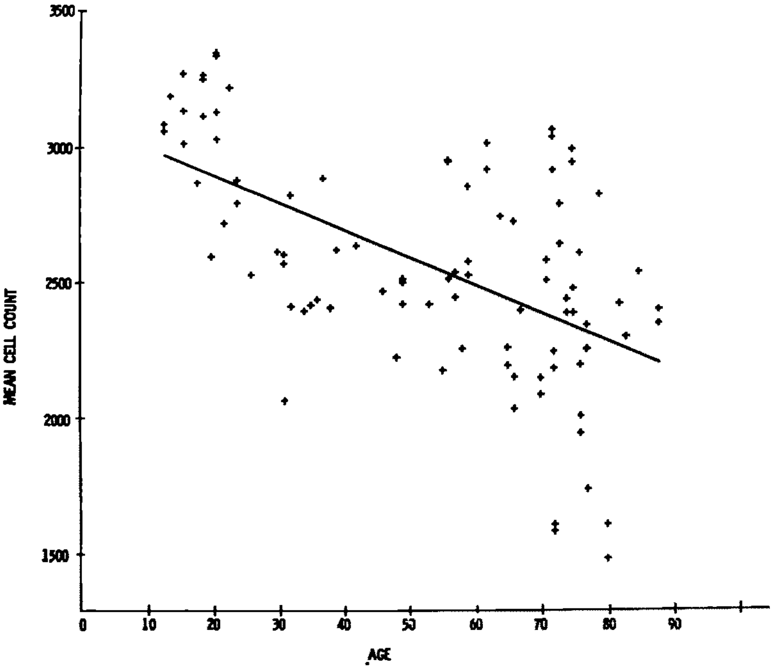

Fig. 6 *Graph showing decrease in mean endothelial cell count with increasing age; 97 eyes*

between the first and second mean cell counts for each eye (Fig. 4) showed a high degree of reproducibility ($P<0{\cdot}001$).

AXIAL VERSUS PERIPHERAL COUNTS

In 9 eyes (9 subjects, aged 20 to 85 years) endothelial cell counts were performed at 3 different sites on the cornea—in the axial region and 3·5 to 4 mm from the nasal and temporal limbus respectively, in the horizontal meridian. A comparison between the mean axial, nasal, and temporal counts showed the following relationships: Axial count $2{\cdot}8\%<$ nasal count ($P<0{\cdot}02$); axial count $3{\cdot}6\%<$ temporal count ($P<0{\cdot}005$); nasal count $0{\cdot}8\%<$ temporal count ($P<0{\cdot}005$).

RIGHT/LEFT CONCORDANCE

Axial endothelial cell counts were performed on both eyes of 31 subjects (15 males, 16 females, aged 13 to 88 years). A comparison between the mean cell counts from the right and left eyes of each subject (Fig. 5) showed close agreement ($P<0{\cdot}001$).

COUNT VERSUS AGE

The relationship between axial cell count and age was studied in a group of 67 subjects comprising 33 males and 34 females, aged between 13 and 88 years. Both eyes were photographed in 30 subjects and only 1 eye in the remainder, so that a total of 97 mean cell counts were plotted against age (Fig. 6). The mean cell count was found to decrease significantly ($P<0{\cdot}001$) with increasing age of the subject. However, a broad range of mean cell counts was found in all age groups, as can be seen from the graph.

The scatter of the 7 to 10 different cell counts recorded from each individual cornea was quantitated by expressing the difference between the highest and lowest counts in each cornea as a percentage of the mean cell count for that cornea. The cell count scatter in 97 corneas varied between 3 and 39%, with a mean value of 14·3%. The influence of subject age and mean cell count on the count scatter in individual corneas is shown in Tables 1 and 2.

Table 1 *Subject age and count scatter*

	Under 50 years old (40 eyes)	*50 years and over (40 eyes)*
Cell count scatter (mean)	12·3%	14·7%
	(8·1 photos)*	(7·7 photos)*

*Mean number of photographs counted per cornea

Table 2 *Mean cell count and count scatter*

	Less than 2500 cells/mm² (40 eyes)	*2500 cells/mm² and over (40 eyes)*
Cell count scatter (mean)	15·6%	12·4%
	(8·5 photos)*	(8·1 photos)*

*Mean number of photographs counted per cornea

Discussion

The technique of endothelial cell counting proved to be highly reproducible when 16 eyes were rephotographed and recounted after an average interval of 7 weeks. Validation of the counting technique is important because the number of cells included in each photograph (40 to 100) is extremely small compared with the total endothelial population of approximately 400 000 cells (Svedberg and Bill, 1972). Furthermore, there can be considerable regional variations in cell size, particularly in older corneas with a low cell density. Finally, it is impossible to be certain that each of the 7 to 10 photographs taken per cornea represents a different area of cells. In practice the involuntary small eye movements of the subject are relied upon to achieve random sampling of the endothelium.

It is technically most convenient to photograph and count the endothelial cells in the axial region, which is clinically the most important part of the cornea. However, the assumption that the axial cell count is representative of the cell density elsewhere in the endothelium has until now never been substantiated. Indeed Irvine (1956) found that the endothelial cell concentration in the centre of the cornea was between 6 and 48% (average 16%) less than at the periphery. He counted endothelial cell nuclei in flat corneal sections from necropsy eyes, however, so that post mortem changes and preparation artefacts cannot be excluded. In the present study peripheral and axial cell counts obtained *in vivo* showed much closer agreement, the axial count being on average only 3·2% lower than the peripheral (nasal and temporal) count. Thus axial cell counts provide a good indication of the total endothelial cell density in the normal cornea. However, following trauma such as that caused by lens extraction, for example, endothelial cell loss is almost certainly unevenly distributed, and axial photography alone cannot be relied upon to quantitate the total endothelial cell population.

Although there is considerable variation in the cell count between individuals of the same age, the variation between the 2 normal eyes of any one individual is extremely small. This raises the possibility of quantitating retrospectively the effects of uniocular trauma on the endothelial cell population by using the unaffected, and presumably normal, eye as a control. Thus, if a traumatised eye required further surgery, knowledge of the cell loss already sustained might influence the choice of surgical procedure.

The gradual decrease in endothelial cell count with increasing age which this study has shown confirms the findings of other workers (Bourne and Kaufman, 1976a; Laing *et al.*, 1976a). An earlier histological study of necropsy eyes had failed to show any clear correlation between endothelial cell density and age (Irvine and Irvine, 1953). The reduced cell counts found in older subjects implies that over the years there occurs a gradual loss of cells which the endothelium cannot adequately replace. Indeed, available evidence suggests that if endothelial cell division does occur in man it is very infrequent (Kaufman *et al.*, 1966). Thus the concept that the corneal endothelial cell reserve is limited should be constantly borne in mind during any surgical manipulations within the anterior chamber.

The normal endothelial cell count varies within wide limits in all age groups so far investigated. Thus some subjects with apparently normal corneas may have cell counts which are between 800 and 1000 cells/mm^2 less than counts in other subjects of the same age. In practical terms this means that the occurrence of diffuse cell loss in a cornea with an initially high cell density might not be detected by a cell count unless the loss was excessive. However, cell loss may be suspected in the presence of marked cell pleomorphism (Sturrock, personal observation). Furthermore, unilateral cell loss can be readily diagnosed by demonstrating a higher count in the fellow eye.

On the assumption that the lower cell counts found in older corneas are indeed due to the gradual loss of cells throughout life it is interesting to speculate why adult corneas of the same age should show such a wide range of endothelial cell densities. This variation may simply reflect a similar variation in cell density already present at birth. Alternatively, the rate at which cells 'drop out' over the years may vary from one individual to another. This would presuppose less variation in endothelial cell density in infants, but specular microscopy has not yet been performed in this age group. Long-term follow-up studies to document changes in cell density occurring in individuals over periods of years would be of considerable interest. Whether the apparent cell loss is genetically predetermined or results from environmental influences such as subtle alterations in aqueous composition and circulation remains to be investigated.

In vivo corneal specular microscopy has now been established as a practical and reliable method for determining endothelial cell density. There are, however, certain limitations to the use of the specular microscope.

Although the technique is fairly simple, counting endothelial cells is time-consuming. However, if the specular microscope is used merely for *in vivo* examination of the endothelium (without taking photographs for subsequent cell counting) it is not always possible to visualise the cells adequately owing to constant small movements of the eye in some subjects. Then it is necessary either to take photographs which can be studied later or use a suction contact lens (Laing *et al.*, 1975), but the latter restricts the examination to the centre of the cornea.

The information obtained from specular microscopy is basically morphological and gives little indication of the functional capacity of the endothelium to maintain corneal deturgescence. Furthermore, absolute cell counts are of limited value, since the minimum cell density compatible with corneal clarity is unknown, and indeed this hypothetical figure probably depends upon the health or 'pumping capacity' of the cells. It has been found that the cornea can remain thin and clear when the axial cell density has fallen to less than 500/mm^2 (Bourne and Kaufman, 1976b; Binkhorst *et al.*, 1977).

It would clearly be of great interest to be able to study selected areas of endothelial cells over prolonged periods of time (days or weeks). Although the changing appearance of individual cells in the rabbit endothelium have been followed *in vivo* for periods of up to 9 hours (Sherrard, 1976), *in vivo* studies in man are impracticable owing to the combination of high magnification, eye movement, and the relative uniformity of the endothelium, which make orientation impossible.

Lastly it is possible to perform specular microscopy only when the cornea is optically clear. Thus the presence of oedema, scarring, or infiltration of the cornea precludes examination of the underlying endothelium. The precise role of corneal endothelial specular microscopy in clinical ophthalmology has yet to be defined, but it clearly represents a significant advance in our ability to study this vital layer of cells.

Statistical analysis of the cell counts was performed by Mr H. Donovan, Institute of Ophthalmology. Thanks are due to Professor Barrie Jones for permission to examine and photograph patients under his care.

References

Binkhorst, C. D., Loones, L. H., and Nygaard, P. (1977). The clinical specular microscope. *Documenta Ophthalmologica*, **44**, 57–75.

Bourne, W. M., and Enoch, J. M. (1976). Some optical principles of the clinical specular microscope. *Investigative Ophthalmology*, **15**, 29–32.

Bourne, W. M., and Kaufman, H. E. (1976a). Specular microscopy of human corneal endothelium in vivo. *American Journal of Ophthalmology*, **81**, 319–323.

Bourne, W. M., and Kaufman, H. E. (1976b). Endothelial damage associated with intraocular lenses. *American Journal of Ophthalmology*, **81**, 482–485.

Bourne, W. M., and Kaufman, H. E. (1976c). Cataract extraction and the corneal endothelium. *American Journal of Ophthalmology*, **82**, 44–47.

Bourne, W. M., McCarey, B. E., and Kaufman, H. E. (1976). Clinical specular microscopy. *Transactions of the American Academy of Ophthalmology and Otolaryngology*, **81**, 743–753.

Irvine, A. R. (1956). The role of the endothelium in bullous keratopathy. *Archives of Ophthalmology*, **56**, 338–351.

Irvine, A. R., and Irvine, A. R. (1953). Variations in normal human corneal endothelium. *American Journal of Ophthalmology*, **36**, 1279–1285.

Kaufman, H. E., Capella, J. A., and Robbins, J. E. (1966). The human corneal endothelium. *American Journal of Ophthalmology*, **61**, 835–841.

Laing, R. A., Sandstrom, M. M., and Leibowitz, H. M. (1975). In vivo photomicrography of the corneal endothelium. *Archives of Ophthalmology*, **93**, 143–145.

Laing, R. A., Sandstrom, M. M., Benospi, A. R., and Leibowitz, H. M. (1976a). Changes in the corneal endothelium as a function of age. *Experimental Eye Research*, **22**, 587–594.

Laing, R. A., Sandstrom, M. M., Benospi, A. R., and Leibowitz, H. M. (1976b). Morphological changes in corneal endothelial cells after penetrating keratoplasty. *American Journal of Ophthalmology*, **82**, 459–464.

Maurice, D. M. (1968). Cellular membrane activity in the corneal endothelium of the intact eye. *Experientia*, **24**, 1094–1095.

Sherrard, E. S. (1976). The corneal endothelium in vivo its response to mild trauma. *Experimental Eye Research*, **22** 347–357.

Svedberg, B., and Bill, A. (1972). Scanning electron microscopic studies of the corneal endothelium in man and monkeys. *Acta Ophthalmologica*, **50**, 321–336.

Vogt, A. (1919). Die Sichtbarkeit des lebenden Hornhautendothels im Lichtbüschel der gullstrandschen Spaltlampe. *Klinische Monatsblätten für Augenheilkunde*, **63**, 233–234.

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Effects of intraocular miotics on cultured bovine corneal endothelium

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SUMMARY Two cases of severe corneal oedema occurred after the use of intraocular pilocarpine. Experimental investigations were conducted with cultured bovine corneal endothelial cells exposed for 5 minutes to 1% pilocarpine solutions of varying composition. Cells were destroyed in solutions not isotonic with aqueous humour, and calcium-free ionic solutions caused loss of cell adhesion without loss of viability. Low pH or the presence of 1% pilocarpine had no detectable effects; 1% acetylcholine chloride in 5% mannitol (Miochol) also caused cell destruction, and this preparation was found to be considerably hypertonic. The minimum requirements for the formulation of intraocular miotics are discussed.

Corneal oedema after operation for cataract is usually an iatrogenic disorder caused by mechanical and chemical injury to the endothelium of the cornea. This investigation was carried out after 2 cases of severe corneal oedema had followed the accidental use of an inappropriate intraocular miotic. The preparation used was a sterile, preservative-free solution of 1% pilocarpine nitrate in water in a single-dose container (Minims, Smith & Nephew Pharmaceuticals Ltd.). This miotic has a pH of 4·5 and an osmolality of approximately 78 mOs/litre and is not designed for intraocular use.

Experiments were set up to study the morphological changes induced in bovine corneal endothelial cell culutures *in vitro* after a brief exposure to various miotic preparations. The relative toxic effects of pH, osmolality, absence of calcium, or presence of pilocarpine were investigated. The probable cause of the corneal oedema noted in the 2 clinical cases included in this report was identified, and the minimum requirements for the formulation of a miotic solution for intraocular use are outlined.

Case reports

CASE 1

An apparently uncomplicated intracapsular cryoextraction for presenile nuclear cataract was performed on a 51-year-old woman. Preoperative examination of the cornea by specular reflection with the slit-lamp microscope had shown slight cornea guttata but an otherwise healthy endothelial mosaic. At the end of the operation the anterior chamber was reformed with a sterile solution of 1% pilocarpine nitrate in water without preservative (Minims). On the first postoperative day severe corneal oedema was present (Fig. 1) and only a 1-mm peripheral band of the inferior part of the cornea remained clear. The eye healed quickly without further complication, but after 7 months there had been no improvement in the bullous keratopathy.

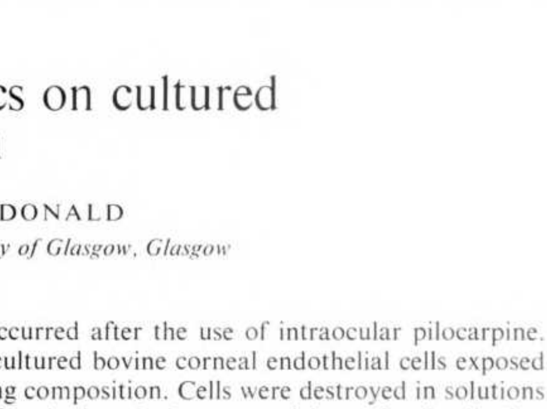

Fig. 1 *Severe corneal oedema 24 hours after intracapsular lens extraction; 1% pilocarpine nitrate in water had been used as an intraocular miotic (Case 1)*

CASE 2

A 69-year-old woman had a similar procedure performed by the same surgeon on the same operating list. Again preoperative assessment of the

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Table 1 *Miotic solutions and their effect on bovine corneal endothelial cell cultures*

Solution	*pH*	*Osmolality (mOs/litre)*	*Number of experiments*	*Effect*	
				Cytotoxic	*Rounding*
1% pilocarpine in water	4·5	81	5	4	0
1% pilocarpine isotonic in NaCl	4·6	282	5	0	3
1% pilocarpine isotonic in NaCl with $CaCl_2$*	4·6	308	3	0	0
1% pilocarpine isotonic in PBS†	7·2	300	5	0	4
Isotonic PBS	7·9	296	4	0	2
1% acetylcholine in 5% mannitol‡	6·0	430	8	4	0
5% mannitol	7·5	292	4	0	0

*Calcium chloride 200 mg/l (anhydrous). †Phosphate buffered saline ($NaH_2PO_4 . 2H_2O/Na_2 HPO_4 . 12H_2O$). ‡Miochol (Cooper Laboratories)

corneal endothelium showed mild guttate change on the endothelial surface but no gross disturbance of the endothelial cell pattern. The anterior chamber was reformed with an identical solution of pilocarpine. Severe oedema of the whole cornea was seen on the first postoperative day, but during the following 3 months the oedema cleared slowly from below. Observation of the corneal endothelium after the oedema had cleared showed severe guttate changes with a distorted cell mosaic. The unoperated eye showed a normal endothelial cell pattern.

Material and methods

Adult bovine corneas were removed from eyes obtained at the local slaughterhouse. Within 4 hours of death the endothelial cell layer together with Descemet's membrane was separated by dissection as described by Stocker *et al.* (1958). The membrane was cut into small pieces with scissors and transferred to plastic tissue culture flasks of 25 cm² surface area. Hepes buffered TC 199 culture medium was used with 10% fetal calf serum and benzyl penicillin 100 units/ml. The cultures were maintained at 37°C. Secondary cultures were obtained by trypsinisation of primary explants with 5% trypsin in calcium- and magnesium- free phosphate buffered saline (Dulbecco's). Tests were performed on established cell cultures which had been maintained for more than 1 year and also on fresh cultures only a few weeks old.

To imitate the time scale of a single dose of intraocular miotic experiments were designed to study the endothelial cell changes after a 5-minute exposure to various test solutions and during 24 hours of recovery in culture medium. 2 ml of test or control solutions (Table 1) were exchanged for the culture medium in each flask and allowed to remain in contact with the cell monolayer for 5 minutes. The solution was poured off and the cells washed with 2 ml of TC 199. The cells were then allowed to recover in the growth medium described above. Four fields in each flask were marked for photography and a series of phase-contrast photomicrographs were taken of each field. The time intervals were: before exposure to the solution, after 5 minutes' exposure, after 2 hours' recovery in growth medium, and after 24 hours' recovery. The entire experiment was carried out in a hot room at 37°C, and during each experiment several different test solutions were compared with control preparations.

The photomicrographs were printed at ×300 magnification and with the identity of the test solution masked; changes in the appearance of the cells in each sequence were recorded. When the analysis of the photographs was complete, the solutions were identified.

Test solutions were made up as shown in Table 1 so that possible toxic effects of osmolality, pH, absence of calcium ions, or presence of pilocarpine could be differentiated. Osmolality was determined by depression of freezing point using a model 3D 'Advance' osmometer, and pH was measured on a blood gas analyser. For the purposes of comparison the commercial preparation of 1% acetylcholine chloride in 5% mannitol (Miochol, Cooper Laboratories) was also tested, as was an isotonic solution of 5% mannitol. A pilot experiment included sterile distilled water as one of the test fluids.

Results

MORPHOLOGICAL CHANGES IN CULTURED ENDOTHELIUM

Two distinct changes in cell morphology were noted in the cultures. Some solutions produced cell destruction which was not obvious at the end of the

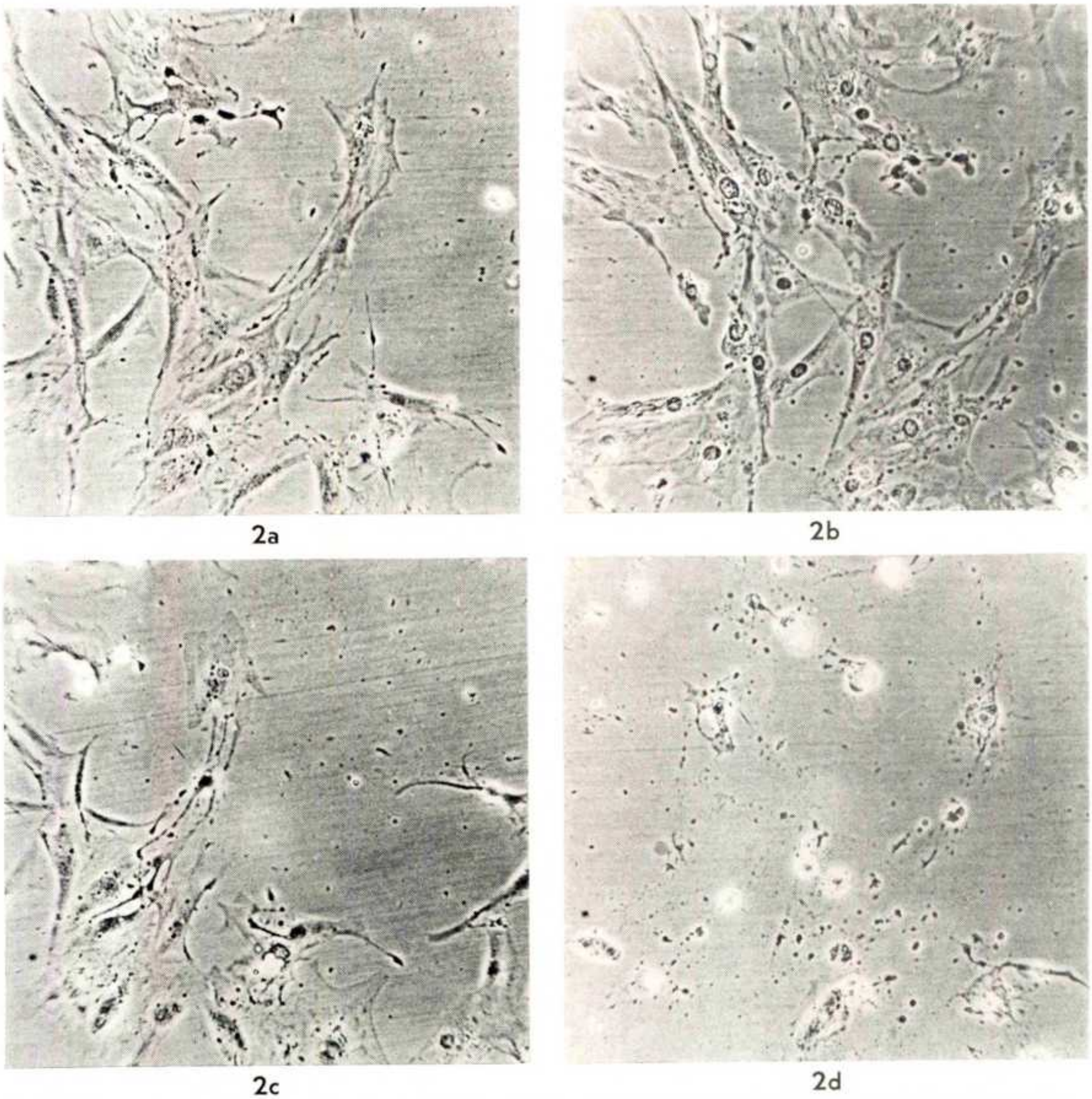

Fig. 2 *Morphological changes in subcultured bovine corneal endothelial cells induced by exposure to 1% pilocarpine nitrate in water; pH 4·5, 81 mOs/l. for 5 minutes. (a) Before exposure, the polygonal cell forms are typical of actively spreading endothelium. (b) The same cells after 5 minutes' exposure; the nuclei are much more prominent and a perinuclear halo is seen. (c) After 2 hours' recovery in TC 199 culture medium the cells show some cytoplasmic disruption. (d) At 24 hours severe cell destruction has occurred (phase contrast, × 100)*

5 minutes' exposure but developed during the subsequent 24 hours in normal growth medium. This is called the cytotoxic effect (Fig. 2). Other test solutions caused the cells to lose adhesion and separate from each other and from the substrate. This is described as cell rounding, and it occurred as soon as the solutions were added to the culture flasks. Residual cells rapidly regained their normal morphology during the recovery phase (Fig. 3).

These changes were seen both in actively dividing areas at the edges of cell colonies and in confluent areas at the centre of the colonies, but the active cell forms showed more marked changes of either type. Recently established cultures seemed just as

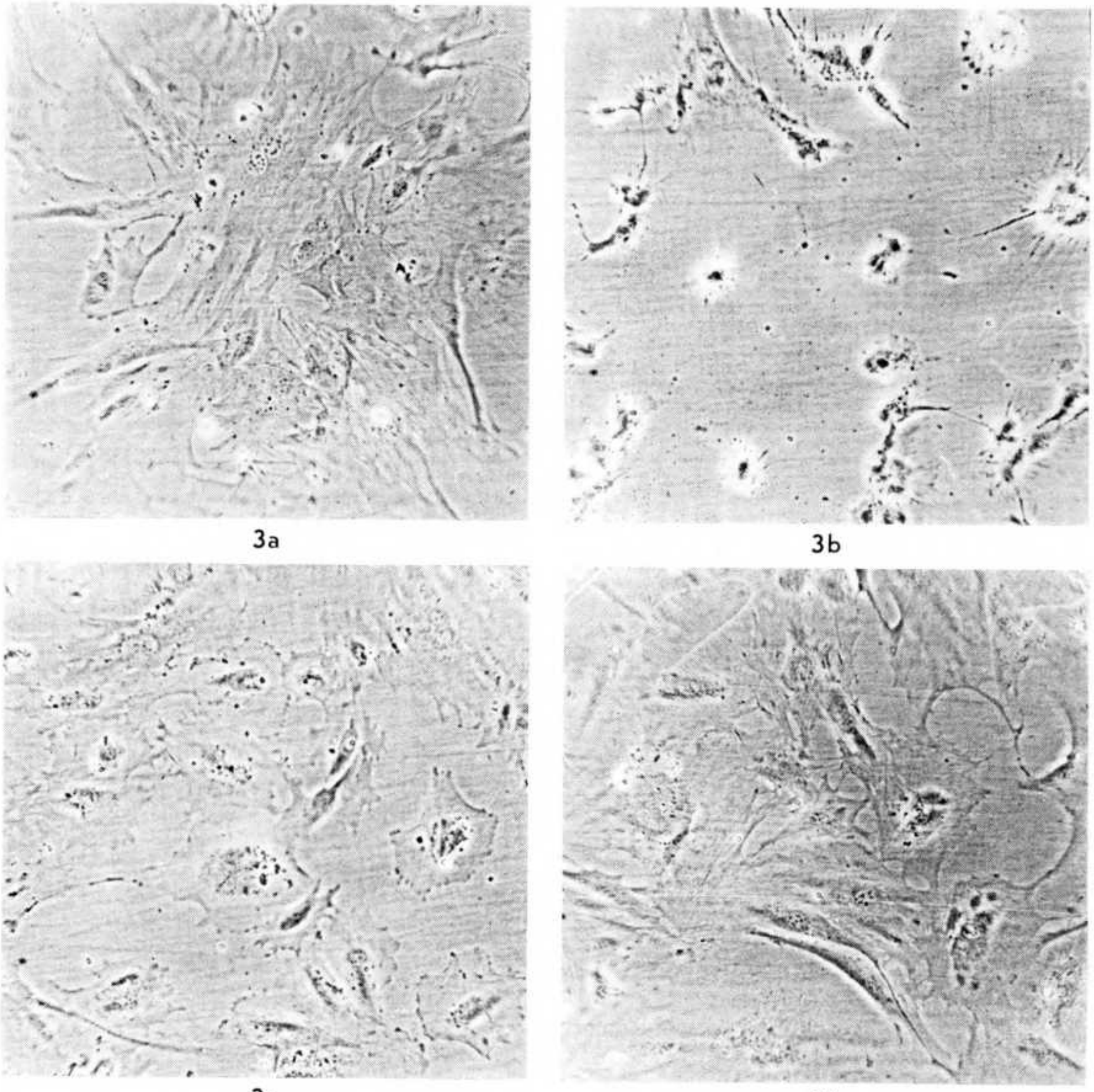

Fig. 3 *Response of subcultured bovine endothelial cells to calcium-free ionic solutions. (a) Initial appearance. (b) The same area after 5 minutes' exposure to 1% pilocarpine nitrate isotonic in sodium chloride. Cells lose adhesion to the substrate and become rounded. (c) After 2 hours' recovery in TC 199 culture medium the cells have again flattened and spread out. (d) After 24 hours' recovery (phase contrast, × 100)*

susceptible to the test solution as did cultures which had been established for over a year.

EFFECTS OF SOLUTIONS UNDER INVESTIGATION

Cytotoxic effect.—After 5 minutes' exposure to 1% pilocarpine nitrate in aqueous solution (pH 4·5, 81 mOs/litre) the cells showed increased prominence of nuclei with a clear perinuclear halo (Fig. 2*b*). These cells showed some distruption of cytoplasm in the early recovery period at 2 hours (Fig. 2*c*), and by 24 hours (Fig. 2*d*) appreciable cell death had occurred. Similar but more severe changes occurred when the cells were exposed to distilled water.

1% acetylcholine chloride in 5% mannitol (Miochol; pH 6·0, 430 mOs/litre) also caused appreciable cell destruction after 24 hours' recovery, although there were no detectable changes in the ealier photographs. Both these preparations causing cell damage had subjected the cells to considerable osmotic shock.

Rounding.—Exposure to isotonic calcium-free ionic solutions (Table 1) caused the cells to separate, lose adhesion to the substrate, and form spheres which were visible in the 5-minute micrographs (Fig. 3*b*). This did not affect the viability of the cells, as rounded cells still in contact with the substrate rapidly flattened on to the bottom of the flasks during the recovery period (Fig. 3*c* and 3*d*). Again actively spreading cells showed greater changes than did confluent cell areas at the centre of colonies.

Table 1 shows that the cytotoxic effects occurred only in non-isotonic solutions while rounding occurred only in isotonic calcium-free ionic solutions. The experiment did not show any identifiable changes which could be attributed to the low pH of some solutions or to the presence of pilocarpine.

1% pilocarpine isotonic in sodium chloride with 200 mg of calcium chloride per litre, pH 4·5, had no detectable effect on the cells after 5 minutes' exposure. An isotonic solution of 5% mannitol was also without effect.

Discussion

The experimental results suggest that the severe corneal oedema which occurred after the 2 cases of intracapsular lens extraction was related to the extreme osmotic shock which was caused by the intraocular use of a solution of 1% pilocarpine nitrate in water. The presence of pilocarpine when isotonic in saline with added calcium had no detectable effect on bovine endothelial cell cultures after 5 minutes' exposure, but after several hours' exposure to pilocarpine a dose-related toxic effect does occur (Coles, 1975a).

Addition of a phosphate buffer to neutralise the rather acid pilocarpine solutions showed no detectable benefit and may have accelerated the rounding effect by combining with residual calcium in the cells to enhance the effect of a calcium-free solution. Buffered preparations would have the disadvantage of rendering the miotic unstable, as pilocarpine in neutral solution undergoes spontaneous isomerisation to inactive isopilocarpine after a few weeks of storage at room temperature (Anderson and Cowle, 1968). The theoretical benefit of using a neutral pilocarpine for intraocular injection would have to be balanced by the risk of cold shock to the corneal endothelium if the buffered pilocarpine required storage at low temperature.

Although it has been shown by Kaye *et al.* (1968) that calcium is essential to maintain the junctional complexes of endothelial cells, it is unlikely that the omission of this divalent cation would cause appreciable endothelial cell death. On the other hand the cell rounding and loss of adhesion demonstrated in this study might be a factor in causing temporary disruption of the continuity of the endothelial barrier *in vivo*. With more severe loss of adhesion some cells might separate completely from Descemet's membrane, so that even after recovery there would be a reduction in the endothelial cell population. This might be enough to provoke decompensation in a cornea with an already reduced endothelial cell density.

The damage produced by 1% acetylcholine in 5% mannitol may be related to the hypertonicity of this preparation, but this has not yet been fully clarified. Mannitol alone in isotonic strength (5%) did not seem to cause changes.

Extracapsular lens extraction, phacoemulsification, intraocular lens implantation, and the use of suction cutting instruments in the anterior segment may require prolonged irrigation of the anterior chamber with an artificial aqueous humour. Perfusion fluids should not be toxic to the corneal endothelium, as the use of an unphysiological solution is likely to potentiate any mechanical disruption of the endothelium during the surgical manipulation. A suitable artificial aqueous for prolonged perfusion has been shown by Edelhauser *et al.* (1976) to require a bicarbonated Ringer's solution with added glucose, glutathione, and adenosine (GBR). The same authors suggest that for low volume irrigation of the anterior chamber less favourable fluids such as sodium chloride 0·9% or Ringer-lactate solution might be adequate.

As miotics for intraocular use are likely to bathe the corneal endothelium only for a short time, their formulation need be less complex than that for solutions used for anterior chamber perfusion. There are, however, some important factors to be observed. The pilocarpine should be prepared in a physiological salt solution containing calcium to maintain cell adhesion, and the final osmolality must be near that of aqueous humour, approximately 300 mOs/litre. No bacteriostatic preservative should be used, as these may cause severe endothelial damage. Maurice and Perlman (1977) have shown that benzalkonium chloride in the concentration used in eye drops causes irreversible destruction of rabbit corneal endothelial function after a few seconds of exposure. In addition toxic effects of intraocular epinephrine have been attributed by Hull *et al.* (1975) to the bisulphate preservative rather than the drug itself, and Coles (1975b) has shown that the endothelial damage caused by erythromycin is aggravated by the addition of benzyl alcohol preservative.

Autoclave sterilisation is suitable for pilocarpine and may be preferable to filter sterilisation, as some membrane filters are coated with a detergent wetting agent which can damage cell cultures if the filters are not washed thoroughly before use. Alternatively, grades of filters specifically for tissue culture media may be used, as these have the wetting agent omitted (Mulvany, 1972).

References

Anderson, R. A., and Cowle, J. B. (1968). Influence of pH on the effect of pilocarpine on aqueous dynamics. *British Journal of Ophthalmology*, 52, 607–611.

Coles, W. H. (1975a). Pilocarpine toxicity. *Archives of Ophthalmology*, 93, 36–41.

Coles, W. H. (1975b). Effects of antibiotics on the in vitro rabbit corneal endothelium. *Investigative Ophthalmology*, 14, 246–250.

Edelhauser, H. F., van Horn, D. L., Schultz, R. O., and Hyndiuk, R. A. (1976). Comparative toxicity of intraocular irrigating solutions on the corneal endothelium. *American Journal of Ophthalmology*, 81, 473–481.

Hull, D. S., Chemotti, M. T., Edelhauser, H. F., van Horn, D. L., and Hyndiuk, R. A. (1975). Effect of epinephrine on the corneal endothelium. *American Journal of Ophthalmology*, 79, 245–250.

Kaye, G. I., Mishima, S., Cole, J. D., and Kaye, N. W. (1968). Studies on the cornea. VII. Effects of perfusion with a calcium-free medium on the corneal endothelium. *Investigative Ophthalmology*, 7, 53–66.

Maurice, D., and Perlman, M. (1977). Permanent destruction of the corneal endothelium in rabbits. *Investigative Ophthalmology*, 16, 646–649.

Mulvany, J. G. (1972). Sterile filtration. In *Animal Tissue Culture: Advances in Technique*, p. 27. Edited by G. D. Walsey. Butterworths: London.

Stocker, F. W., Eiring, A., Giorgiade, R., and Giorgiade, N. (1958). A tissue culture technique for growing corneal epithelial, stromal, and endothelial tissues separately. *American Journal of Ophthalmology*, 46, 294–298.

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Cogan's microcystic dystrophy of the cornea: ultrastructure and photomicroscopy

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SUMMARY Corneal biopsy specimens from 3 patients with Cogan's microcystic corneal dystrophy were examined by light and electron microscopy. Specimens were taken from corneas showing microcysts, geographic or map-like areas, and refractile striae. In all samples there is a bilaminate subepithelial layer of fibrogranular material, the friability of which is probably the basis for recurrent erosions in this disorder. Histochemical and ultrastructural findings provide further evidence that Cogan's dystrophy, the finger print/bleb dystrophy, and Meesmann's dystrophy should be regarded as separate entities.

In their original account of microcystic dystrophy Cogan *et al.* (1964) noted bilateral white dots, about 0·1 to 0·05 mm wide, within the corneal epithelium of 5 unrelated patients. The presumably spontaneous appearance of these dots in adult life, together with the absence of inflammatory signs, naturally suggested an abiotrophic basis for the disorder. In the following year Guerry (1965) supplemented Cogan and colleagues' description by noting that the dots were accompanied by relucent, often subtle, map-like or 'geographic' nebulae which lay anterior to Bowman's membrane. These map-like patches are in fact the essential biomicroscopic feature of this condition, since they are often present without microcysts. In the same year Bietti's (1965) 'lacunar dystrophy' was apparently an independent account of the same disorder. There is general agreement that the dots, and to some extent the map areas, are in a constant state of flux, disappearing or new ones spontaneously appearing often within a few days. Support for a dystrophic aetiology was provided by Laibson and Krachmer (1975), whose studies show familial incidences suggesting autosomal dominance. Although many patients with this disorder are asymptomatic, others experience annoying symptoms either of epithelial breakdown or, if the opacities lie in the central cornea, of irregular astigmatism and diffraction.

The pathological basis of the map areas seems to be the deposition of an abnormal sheet of fibrogranular material which lies at the epithelial level. The microcysts were shown by Cogan and his co-workers (1964) to represent degenerating cells which are surrounded but not engulfed by their neighbours. In these and other respects there are undoubted resemblances between Cogan's dystrophy and the fingerprint/bleb dystrophy described by Bron and Brown (1971). Hence Laibson (1976) considered that the two conditions are essentially variants, though ultrastructural evidence of this contention is fragmentary.

The fine structure of the corneal epithelium in 3 patients with Cogan's microcystic dystrophy is the basis of the present study, in which its pathogenesis and relationship to other superficial dystrophies featuring epithelial microcysts is discussed.

Case reports

CASE 1

A white woman aged 58 years was found to have impaired vision in both eyes associated with bilateral posterior subcapsular cataracts. An intermittent sensation as of a foreign body had been present in both eyes for several months. Irritation of one or other eye accompanied by watering and photophobia would occur at any time of the day and last several hours. The slit-lamp microscope revealed map-like areas in the epithelial layer of both corneas. They were associated with numerous white microcysts on the left side. The map areas were best seen in the oblique broad beam as greyish relucent

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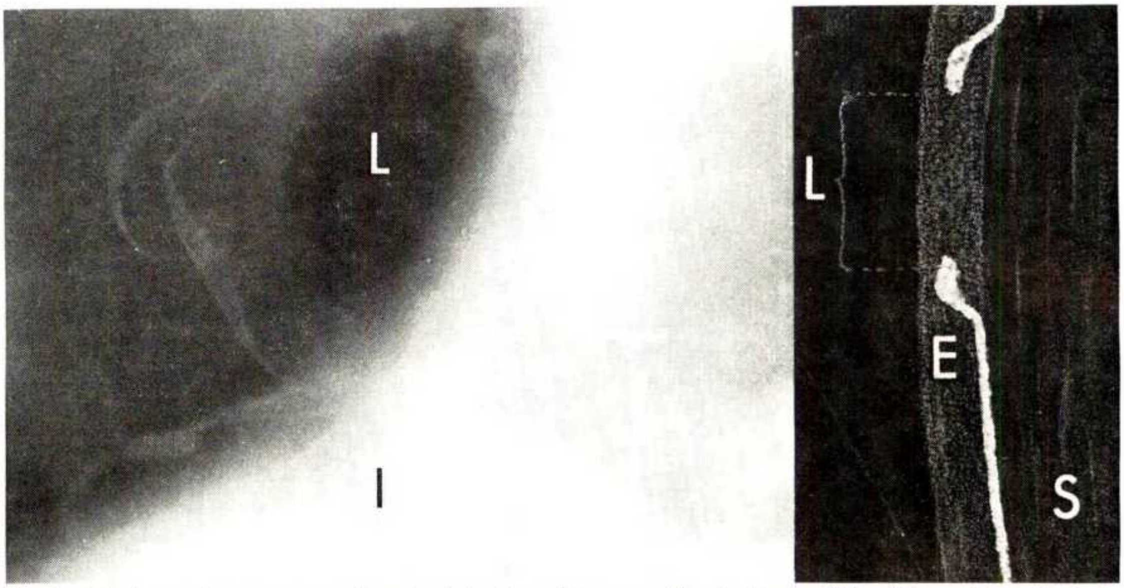


Fig. 1 *Biomicroscopic appearance of 'map' nebulae in pupillary zone. Illumination by oblique light and from iris,* I. *Lacuna,* L, *and rolled edges of map material are displayed.* ×3. *Inset, drawing of optical section of this area,* E, *epithelium;* S, *stroma* ×70

patches irregular in shape and often perforated by round holes a millimetre or so wide (Fig. 1). Details of such a hiatus shown in Fig. 1 underwent no photographically documented change over a 4-month period. The edges of these lacunae were sharply defined and in places seemed rolled over, an appearance which, as noted by Laibson (1976), is reminiscent of the capsular dehiscences seen in 'pseudoexfoliative' disease of the lens. The curled edge was refractile in retroillumination both from the iris and if viewed with the ophthalmoscope against the fundal reflex, when it appeared as a black line. In optical section a bright seam underlies the epithelium and coincides with the map areas. Near the lacunae this seam enters the epithelial band obliquely and terminates, becoming thicker at its free end, where it corresponds with the rolled edge (Fig. 1, inset). In both corneas fine refractile lines were seen by retroillumination from the iris. They differed from those seen in fingerprint dystrophy in that they could also be seen in the direct or focal slit-lamp beam, wherein they were visible as greyish lines. None of these features showed any staining with fluorescein, rose bengal, alcian blue, or iodonitrotetrazolium. The fluorescein-stained tear film rapidly broke up over the refractile striae and over the rolled edge of the geographic patches, probably indicating relative elevation of the corneal surface at these points. Moreover, massaging the cornea through the closed lid resulted in well-defined pools of fluorescein corresponding with these structures. The anterior corneal mosaic was intact. Corneal sensation to No. 7 nylon was unimpaired.

Since removal of the left cataract was indicated, preliminary debridement of the affected corneal epithelium was undertaken 2 months before operation. The regenerated epithelium, although showing new map areas, was free of microcysts, and symptoms of irritation improved. An uneventful left cataract extraction was performed with resultant 20/20 vision. The ablated corneal epithelium and the cataractous lens were placed in fixatives appropriate for subsequent microscopy.

CASE 2

A 40-year-old white woman developed familial cataracts which 3 years ago had advanced to the point when left lens extraction was successfully undertaken. Since then a soft contact lens had been comfortably worn and provided her with 20/20 vision. For the past few years, however, recurrent irritation of the right eye had been accompanied by redness and photophobia. Slit-lamp examination of both corneas showed geographic patches with rolled edges characteristic of Cogan's microcystic dystrophy and with staining characteristics similar to those in Case 1. One or two microcysts were found sporadically in both corneas. A few grey lines resembling those seen in fingerprint dystrophy were

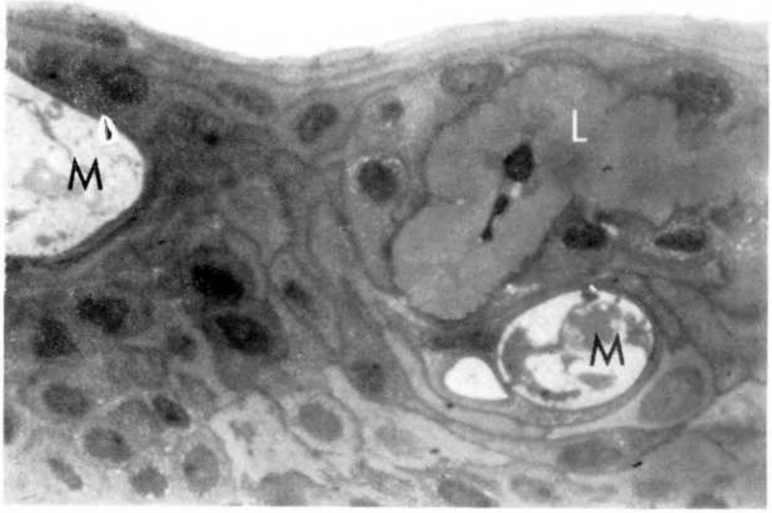


Fig. 2 *Corneal epithelium. Microcysts,* M, *lie near rolled edge of midepithelial lamina,* L. *Epithelial cells in this region appear distorted by the laminal edge. Toluidine blue* × 760

present in each cornea; they were visible in both focal and reversed light. Irritation of the right eye continued in spite of the liberal use of bland ointments, so that limited curettage of the corneal epithelium was undertaken. This was followed by less frequent attacks. The ablated epithelium was preserved for microscopy.

CASE 3

A white woman aged 60 was found to have corrected visual acuities of OD = 20/30 and OS = 20/20. There had been no symptoms suggestive of recurrent epithelial breakdown. Geographic patches of Cogan's microcystic dystrophy as described above were present in both corneas. There were no microcysts but 1 or 2 sheaves of fine grey lines were seen in focal light. A 2-mm trephine was used to obtain an epithelial biopsy from the pupillary zone of the right cornea. Recovery was uneventful, and vision on the right side improved by 1 line.

Methods

Corneal epithelial biopsies from Cases 1 and 2 were fixed in 10% neutral formalin, dehydrated, and then infiltrated with paraffin wax. Paraffin sections were treated with various staining techniques to be mentioned alongside the results.

Other corneal epithelial specimens from all 3 patients were fixed in 2½% cold glutaraldehyde prior to osmification and embedding in epoxy resin. Pieces of the cataractous lens obtained from Case 1 were fixed in 10% neutral formalin, osmified, and embedded in epoxy resin. Orientational sections were stained with toluidine blue and examined with the light microscope while suitably thin sections were stained with uranyl acetate and lead citrate before being submitted to transmission electron microscopy with a Phillips 300 electron microscope.

Observations

LIGHT MICROSCOPY

The lens from Case 1 showed changes consistent with posterior subcapsular cataract. There were no abnormal periodic acid Schiff (PAS) positive accumulations in relation to the lens capsule. Corneal specimens from the 3 patients consisted of epithelium basement membrane and a subepithelial layer of 'hyaline' material. Vacuolar degeneration of the epithelial cells together with acantholytic isolation of individual cells was seen in some sections.

The subepithelial seam was lightly stained pink in haematoxylin and eosin, and although otherwise structureless consisted of a more densely stained superficial layer and a paler deep layer. In places the superficial layer of this seam was insinuated between the epithelial cells and lay at a variable depth as a horizontal lamina between the surface and basal cells. In some areas this lamina was apparently ruptured. The broken ends, which were coiled, suggesting elasticity (Fig. 2), apparently corresponded with the rolled edges of the lacunae seen with the slit lamp (Fig. 1 inset). There was some distortion of the epithelial cells near the rolled edges (Fig. 2), giving the impression that it was conditioning their forward migration. Elsewhere continuity of the midepithelial lamina was maintained until it finally rejoined the subepithelial seam; the epithelial enclave thus isolated contained the majority of the microcysts.

The subepithelial and midepithelial seams were

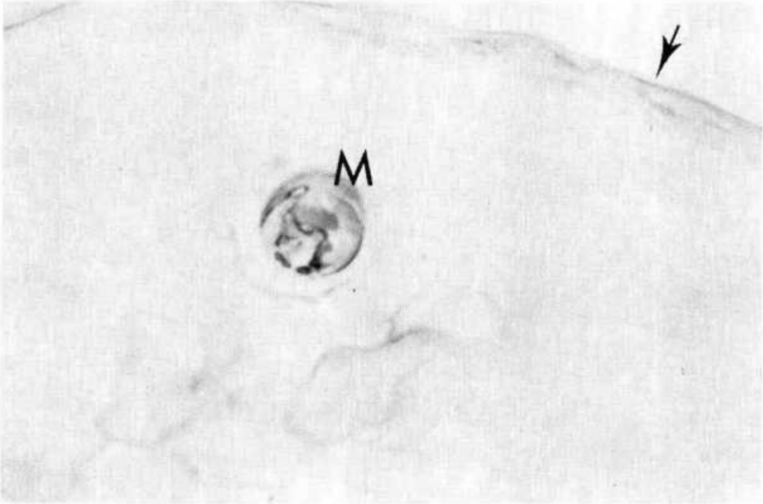


Fig. 3 *Corneal epithelium. Microcyst,* M, *surface squames* (arrowed), *and nearby cell interfaces are stained with alcian blue* ×1070

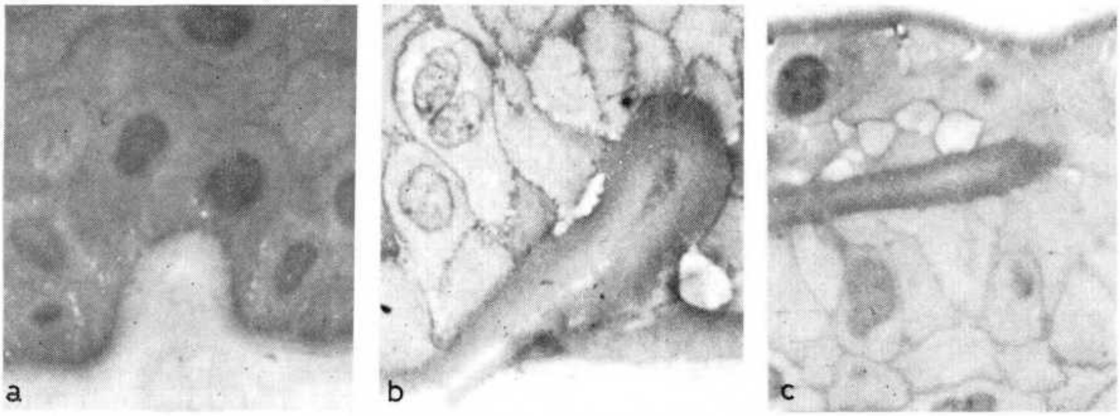


Fig. 4 *Corneal epithelium to show possible pathogenesis of refractile striae.* (a) *Minimal folding of bilaminar subepithelial membrane.* (b) *Oblique invagination of similar fold into the epithelium.* (c) *Horizontal extensions correspond with striae, their duality is still evident. Toluidine blue* ×1100

strongly PAS positive but did not stain with alcian blue or Gomori's reticulin stain. They were monorefringent in polarised light and did not exhibit autofluorescence in ultraviolet light.

Microcysts contained fragmented cell debris which was often PAS positive and invariably stained with alcian blue at pH 2·5 (Fig. 3) and with colloidal iron. The lining surface of the microcysts was regularly stained with alcian blue, colloidal iron, and with Gomori's method for alkaline phosphatase in a manner similar to the anterior corneal surface. Cell borders in the vicinity of the microcysts were often sharply outlined with alcian blue and colloidal iron. Pretreatment of paraffin sections with hyaluronidase or diastase did not prevent or diminish colouration with PAS, alcian blue, or colloidal iron in any of the above structures. In general, the microcysts lay posterior to the midepithelial lamina, but a few lay close to the surface near the ruptured curled-up ends of this structure.

The refractile striae were apparently produced by invagination of the subepithelial seam, a process in which both layers were involved (Fig. 4).

TRANSMISSION ELECTRON MICROSCOPY

Epithelial cells for the most part appeared to be healthy but in places, especially posterior to the midepithelial lamina, varying degrees of hydropic degeneration were seen to result in cytoplasmic pallor. This change was accompanied by acantholy-

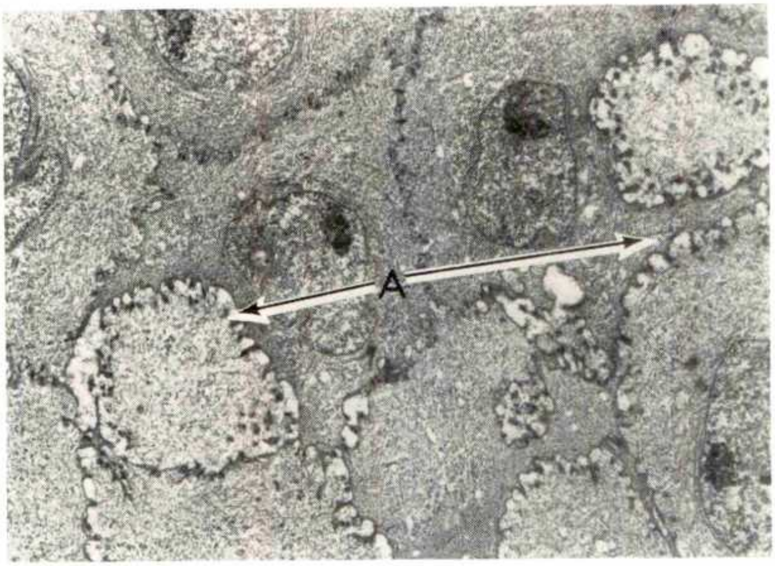


Fig. 5 *Corneal epithelium, 'pale' cells, showing acantholysis,* A, *with intercellular accumulation of granular material* ×3600

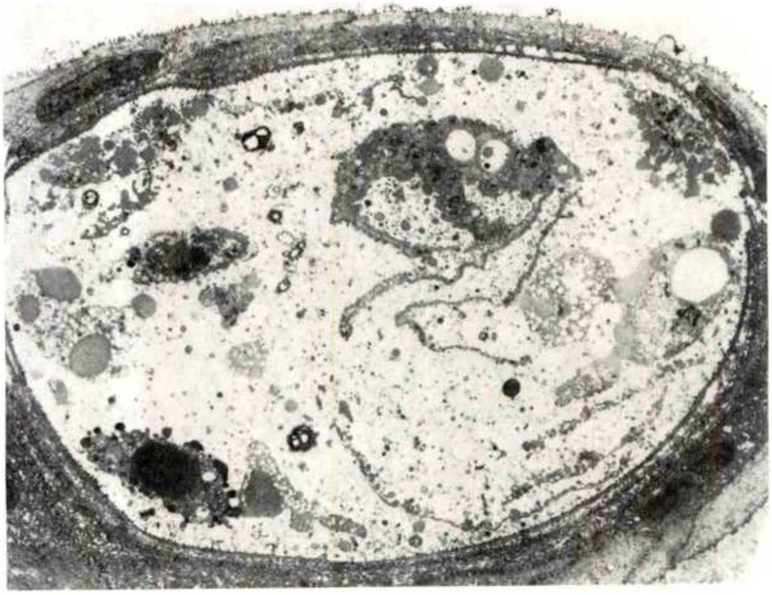


Fig. 6 *Corneal epithelium. Microcyst separated by attenuated squames from tear film. The surface lining of cysts is thrown into microvilli. Cyst contents include cell membranes, myelin figures, granules, and vacuolated cystoplasmic remnants. Montage* ×2100

sis (Fig. 5) with the formation of amorphous granules in the widened interspace, and was presumably followed by cell shrinkage and microcyst formation. Occasionally the basal cells showed fine cytoplasmic processes extending into the subepithelial seam.

Microcysts contained a variety of cell fragments including myelin figures and cell membranes, but organelles were rarely recognisable (Fig. 6). The cell membranes surrounding these cysts were thrown into microvilli similar to those of the surface squames. The midepithelial lamina (Fig. 7) consisted mainly of irregularly banded fibres embedded in granular material similar to the superficial layer of the subepithelial seam with which it was continuous. Basement membrane and hemidesmosomes were sparse. The refractile striae were seen as interepithelial protrusions of both layers of the subepithelial layer and appeared to be produced by folding of this membrane. Basement membrane and

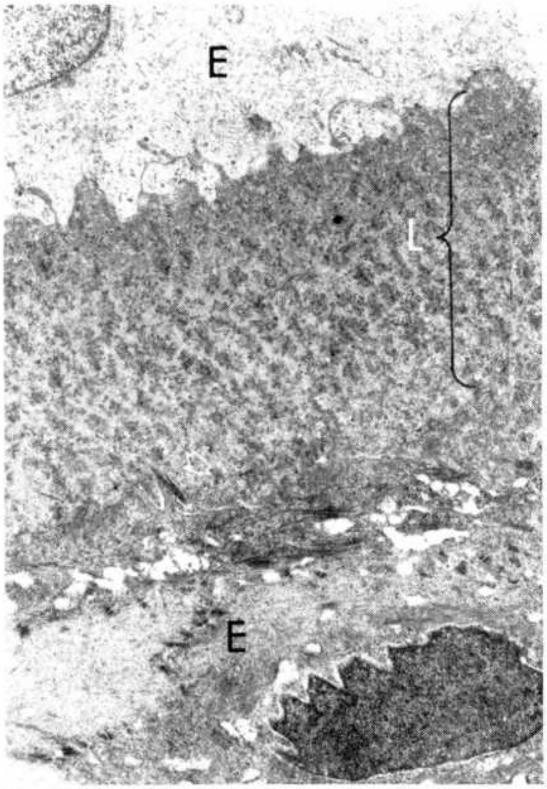


Fig. 7 *Corneal epithelium,* E, *contains midepithelial lamina,* L, *composed of irregularly banded fibres, embedded in granular matrix producing a dappled effect. Basal lamina and hemidesmosomes sparsely present. Occasional collagen-like fibrils* (arrowed) *lie alongside* L × 4270

hemidesmosomes were sporadically present in these infoldings.

The subepithelial seam in all specimens as noted in light microscopy was bilaminate (Fig. 8). A basement membrane was often present and appeared to have its normal complement of hemidesmosomes, but there were places where both elements were absent. The superficial layer consisted of granular material which was intimately connected to the hemidesmosomes (Fig. 9). This material formed a honeycomb-like system of compartments in which lay fibres, some 50 nm long. They were composed of laterally aggregated fibrils 8 nm wide which fanned out in three dimensions at both ends (Figs. 10, 11). The deeper layer was mostly composed of randomly orientated fibrils banded at 28 nm (Fig. 12). They had a dense outer rim and rarefied core when seen in cross-section. Coarser fibrils banded at 66 nm like typical collagen were occasionally interspersed among the finer fibrils (Fig. 13). In some places the deep layer was composed partly of granules measuring about 7 nm.

Discussion

The pathogenesis of Cogan's microcystic dystrophy has recently been discussed by Cogan *et al.* (1974) and by Rodrigues *et al.* (1974). Both groups consider that the microcysts, which are usually found posterior to a midepithelial lamina of presumed aberrant basement membrane material, develop because the forward migration of epithelial cells is now mechanically inhibited by this lamina. Thus trapped, the deeper cells undergo changes *in situ*

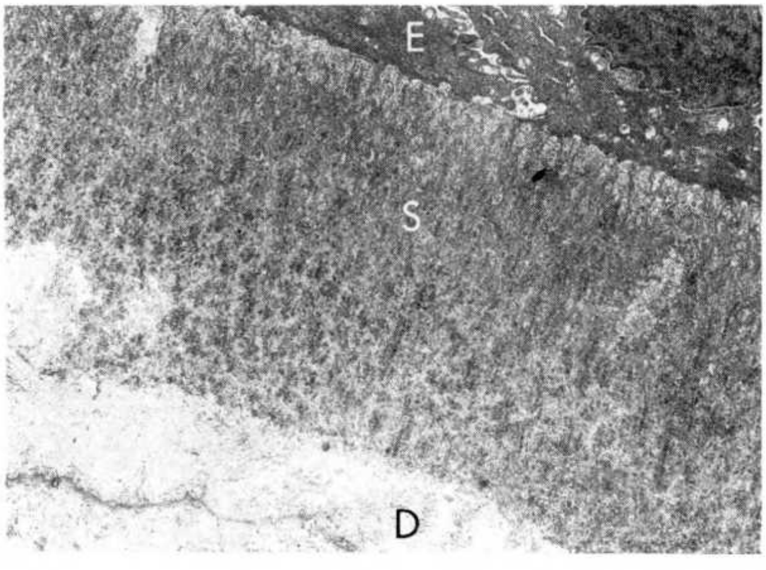


Fig. 8 *Bilaminate seam lies underneath epithelium,* E, *and consists of 2 layers: a superficial stratum,* S, *in which darkly stained fibres are embedded in finely granular matrix, which itself is in continuity with hemidesmosomes; and deep layer,* D, *which is less densely packed and contains finer randomly orientated fibrils* × 3780

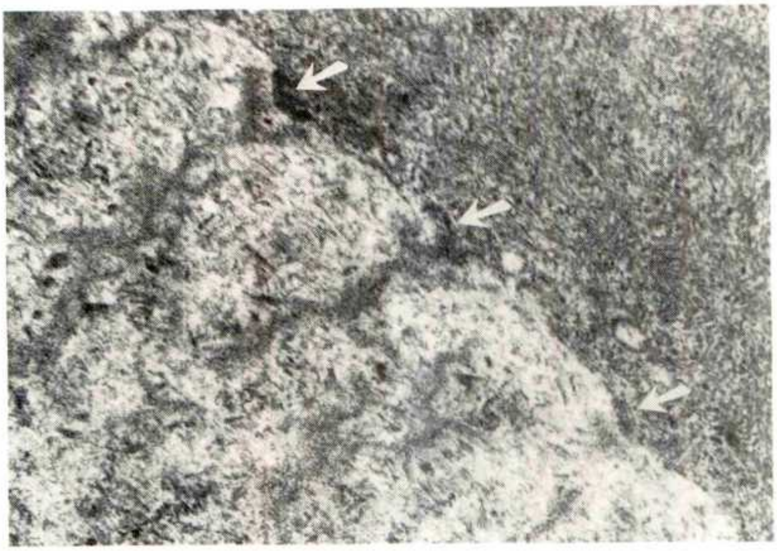


Fig. 9 *Illustrates continuity of basement membrane-like granular material of the superficial layer with hemidesmosomes* (arrowed) ×46 500

which fit them for their normal role as surface squames. Thereafter their programmed death is followed by autolysis and subsequent seclusion as microcysts. The microcysts move forward, probably through lacunae in the midepithelial lamina, and finally their contents erupt into the tear film. The morphological findings of the present study do not contradict this view of the pathogenesis of the microcysts, but it is equally possible that some other factor such as permeability characteristics of the intraepithelial lamina (which are unknown) may result in impaired metabolism of the deeper cells and so contribute to their premature death. Phagocytosis is not involved in the process of microcyst formation, the walls of the cysts being formed by adjacent cells which flatten and surround without engulfing the dying cells. Tripathi and Bron (1973) observed acantholysis of the pale cells as the first discernible sign of cell death, a finding confirmed here. Histochemical findings in the present study suggest that intercellular and surface accumulation of acid mucopolysaccharides may be an early sign of cell upset which precedes microcyst formation. It is of interest in this connection that Skerrow and Matoltsy (1974) found significant quantities of PAS positive glycoproteins in their chemical analysis of isolated desmosomes. These changes are suggestive of a metabolic lesion rather than simply a vicarious maturation due to impaired forward migration. Encystment is apparently followed by dehydration shrinkage and finally autophagic breakdown. Similar morphological observations on the formation of microcysts were made by Broderick *et al.* (1974) in their study of fingerprint dystrophy. A midepithelial sheet of basement-like material is not, however, a feature of fingerprint dystrophy or of the other conditions in which microcysts occur.

Subepithelial basement membrane material was seen in all sections studied and it is presumably present over most of the cornea. It consists of two

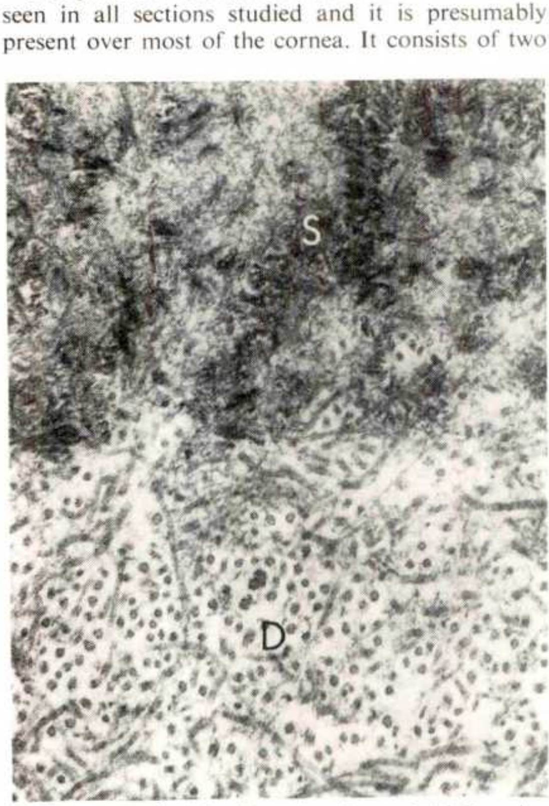


Fig. 10 *Sharply defined junction of superficial,* S, *and deep layer,* D, *of subepithelial material* ×44 270

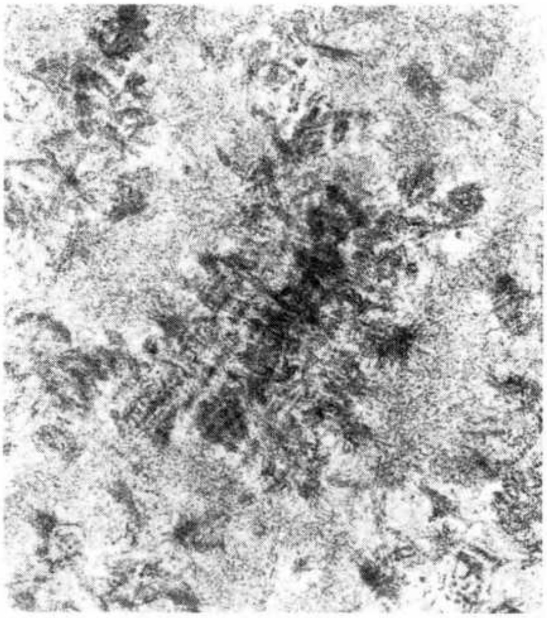


Fig. 11 *Irregularly banded fibre in superficial part of subepithelial seam contains numerous laterally aggregated fibrils 8 nm wide embedded in fine granules* ×88 500

layers. The first is a superficial zone containing fine granular material which is seemingly being synthesised in the vicinity of the hemidesmosomes. This material is compartmented like a sponge, in the cells of which lie peculiar banded fibrils reminiscent of those found by McTigue and Fine (1966) at the periphery of the normal cornea. In places villous projections extend from the basal cells into this layer. The deeper layer consists of banded fibrils which are presumably abnormal type IV collagens. Friability of the abnormal material lying beneath the corneal epithelium appears to be responsible for the ease with which epithelium may be surgically removed in this condition and it is probably the basis for recurrent erosions.

Aberrant basement membrane at the midepithelial level is continuous with the more superficial lamina of the two subepithelial layers and has a similar structure. Cells adjacent to this sheet of fibrogranular material are not otherwise identifiable as basal cells; moreover, hemidesmosomes and normal basement membrane are rarely discernible. This lamina of fibrogranular material appears to be the histological counterpart of the map-like nebulae seen with the slit lamp. The midepithelial extensions of the superficial layer of this basal seam may result from tangential forces causing buckling. Epithelial cells insinuating posterior to this layer go on dividing until the lamina breaks, allowing these cells and the microcysts to erupt into the tear film. Thus in places this layer is ruptured and the free ends curled back in a scroll doubtless corresponding with the biomicroscopic appearances of lacunae with rolled edges (Fig. 1).

Fine refractile lines resembling those seen in fingerprint dystrophy also lie at the midepithelial layer. They are apparently produced by invagination of the subepithelial seam and hence have a multi-

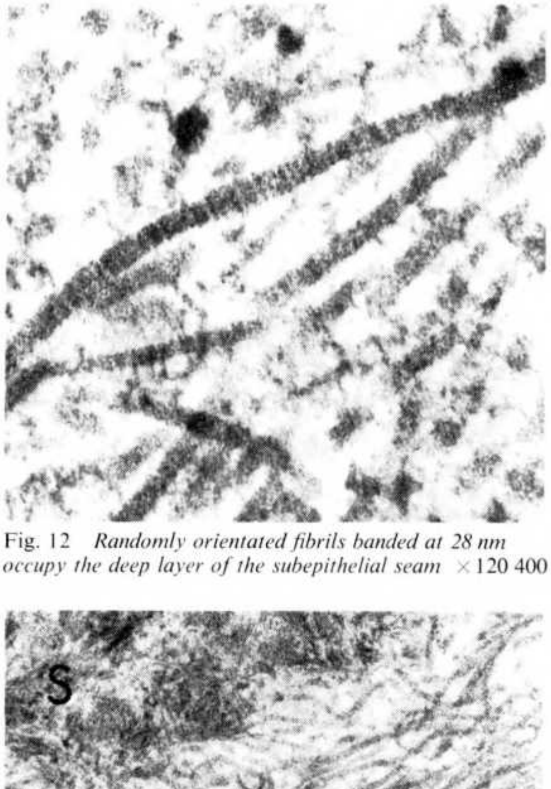


Fig. 12 *Randomly orientated fibrils banded at 28 nm occupy the deep layer of the subepithelial seam* ×120 400

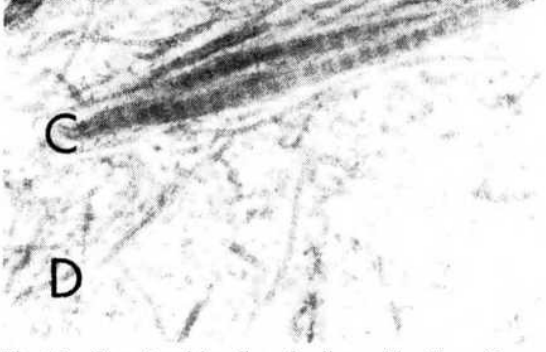


Fig. 13 *Occasional bundles of collagen-like fibres,* C, *banded at 66 nm lie at the junction of the superficial,* S, *and deep,* D, *zones of subepithelial seam* ×52 500

Table 1 *Corneal epithelial diseases with microcysts and abnormal basement membrane production*

'Primary'	*'Secondary'*
Cogan's microcystic dystrophy	H. simplex (Broderick and Dark, 1976)
Meesmann's dystrophy	Trauma (Laibson, 1976)
Fingerprint/bleb dystrophy	Fuchs's corneal dystrophy (Bron and Tripathi, 1973)
	Dysplasia of corneal epithelium (Dark and Streeten, 1978, unpublished observations)

laminar appearance in section. Laibson (1976) noted that they may be the sole manifestation of this disorder in members of some affected kinships. Moreover, since microcysts may occur in fingerprint dystrophy as observed by Broderick *et al.* (1974), Laibson (1976) was led to postulate that map nebulae, microcysts, and refractile striae are a spectral expression of the same fundamental disorder.

In contrast to this view of a continuum the present study serves to emphasise the differences between fingerprint and Cogan's dystrophy. Thus, the subepithelial seam and refractile striae in microcystic dystrophy consist of irregularly banded fibrils embedded in a fine granular matrix, in contrast to the granular ultrastructure of the striae and subepithelial seam seen in fingerprint dystrophy as described by Broderick *et al.* (1974) and the subepithelial seam in bleb dystrophy by Dark (1977). Biomicroscopically the striae in Cogan's dystrophy are visible in focal illumination as fine grey lines unlike those of the fingerprint disorder, which are visible only in retroillumination. Moreover, the large 'putty' cysts of Cogan's dystrophy, as pointed out by Bron and Tripathi (1973), have distinctive morphological and tinctorial properties which set them apart clinically from microcysts seen in a variety of other superficial disorders of the cornea of which Table 1 is an incomplete classification.

A consideration of the histological and cytological findings also serves to delineate the 'primary' disorders of this group. From the present study of Cogan's dystrophy the basic ultrastructural cell change appears to be hydropic cell degeneration, followed by shrinkage with intercellular accumulation of acid mucopolysaccharide (AMP). Fine and his co-workers (1977) have shown that in Meesmann's dystrophy autofluorescent AMP accumulates within both the cell and the abnormal subepithelial seam; moreover, the ultrastructural finding of a 'peculiar' fibrillogranular material in the cytoplasm is diagnostic of this disease. In fingerprint dystrophy Broderick *et al.* (1974) described cell shrinkage and the formation of multinucleated epithelial giant cells as the salient cytological changes. There is thus increasing evidence (Table 2) for tentatively regarding these 3 disorders as separate diseases.

It is a pleasure to acknowledge Miss Sharon Edward's responsibility for the technical aspects of electron microscopy in this study.

This study was supported by a grant from the Research Service of the Veterans Administration.

Table 2 *Comparison of Cogan's, fingerprint/bleb, and Meesmann's dystrophies*

	Cogan	*Fingerprint/Bleb*	*Meesmann*
Epithelial cytology	Intracellular oedema, acantholysis, intercellular accummulation of AMP	Acantholysis, cell shrinkage, epithelial cell fusion	Diagnostic accumulation of fibrillogranular material within cytoplasm
Microcysts			
Biomicroscopy	Large (20 μm to 1 mm) opaque unstained with fluorescein	Translucent or clear (10 to 100 μm) staining with fluorescein	Small stained with fluorescein (10 to 50 μm)
Histochemistry	AMP positive. No autofluorescence. PAS positive	AMP positive.* No autofluorescence.* PAS positive	AMP positive. Autofluorescence. PAS positive
Ultrastructure	Loosely packed amorphous debris	Electron-dense masses	Homogeneous vacuolated substance
Abnormal basement membrane			
Biomicroscopy	Visible direct and retro beam as map nebulae and refractile striae	Visible only in retroillumination as fingerprint striae	Not observed
Histochemistry	AMP negative. PAS positive	AMP negative. PAS positive	AMP positive. PAS positive
Ultrastructure	Fibrogranular	Granular	Fibrogranular and granular

* Dark, A. J., unpublished observations

References

Bietti, G. B. (1965). Contribution à la connaissance des dégénérescences cornéennes seniles. *Archives d' Ophtalmologie et Revue Générale d'Ophtalmologie*, **25**, 37–42.

Broderick, J. D., Dark, A. J., and Peace, G. W. (1974). Fingerprint dystrophy of the cornea: a histologic study. *Archives of Ophthalmology*, **92**, 483–489.

Broderick, J. D., and Dark, A. J. (1976). Fingerprint striae of cornea following herpes simplex keratitis. *Annals of Ophthalmology*, **8**, 481–484.

Bron, A. J., and Brown, N. A. (1971). Some superficial corneal disorders. *Transactions of the Ophthamological Societies of the United Kingdom*, **91**, 13–29.

Bron, A. J., and Tripathi, R. C. (1973). Cystic disorders of the corneal epithelium, I. Clinical aspects. *British Journal of Ophthalmology*, **57**, 361–375.

Cogan, D. G., Donaldson, D. D., Kuwabara, T., and Marshall, D. (1964). Microcystic dystrophy of the corneal epithelium. *Transactions of the American Ophthalmological Society*, **62**, 213–225.

Cogan, D. G., Kuwabara, T., Donaldson, D. D., and Collins, E. (1974). Microcystic dystrophy of the cornea: a partial explanation for its pathogenesis. *Archives of Ophthalmology*, **92**, 470–474.

Dark, A. J. (1977). Bleb dystrophy of the cornea: histochemistry and ultrastructure. *British Journal of Ophthalmology*, **61**, 65–69.

Fine, B. S., Yanoff, M., Pitts, E., and Slaughter, F. D. (1977). Meesmann's epithelial dystrophy of the cornea. *American Journal of Ophthalmology*, **83**, 633–642.

Guerry, D. (1965). Observations on Cogan's microcystic dystrophy of the corneal epithelium. *Transactions of the American Ophthalmological Society*, **63**, 320–334.

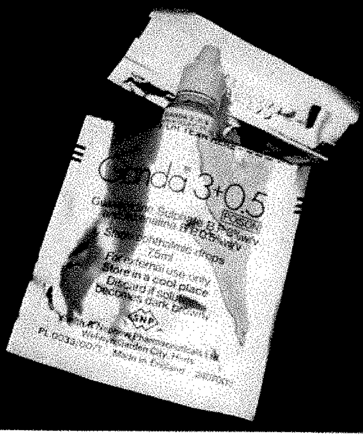
Laibson, P. R., and Krachmer, J. H. (1975). Familial occurrence of dot (microscopic) map, fingerprint dystrophy of the cornea. *Investigative Ophthalmology*, **14**, 397–399.

Laibson, P. R. (1976). Microcystic corneal dystrophy. *Transactions of the American Ophthalmological Society*, **74**, 483–531.

Rodrigues, M. M., Fine, B. S., Laibson, P. R., and Zimmerman, L. E. (1974). Disorders of the corneal epithelium: a clinicopathologic study of dot, geographic and fingerprint patterns. *Archives of Ophthalmology*, **92**, 475–482.

Skerrow, C. J., and Matoltsy, A. G. (1974). Chemical characterization of isolated desmosomes. *Journal of Cell Biology*, **63**, 524–530.

Tripathi, R. C., and Bron, A. J. (1973). Cystic disorders of the corneal epithelium. II. Pathogenesis. *British Journal of Ophthalmology*, **57**, 376–390.



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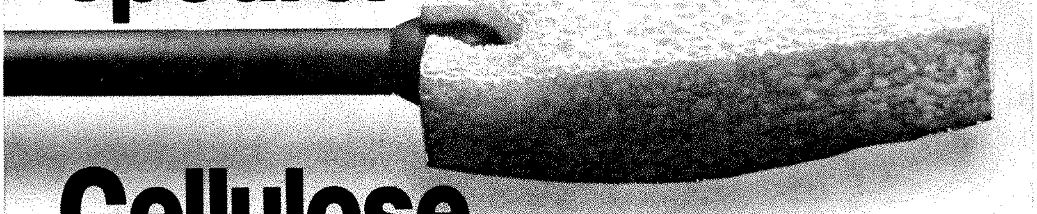

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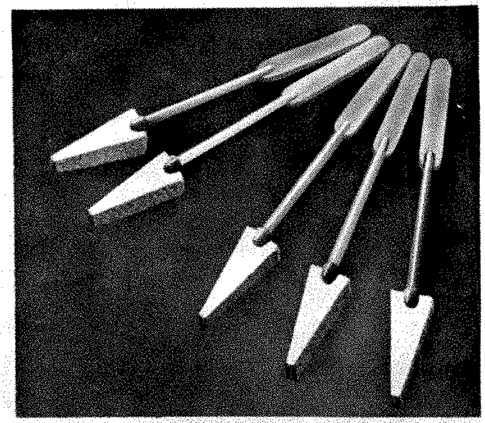

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The reverse Wessely phenomenon: immune corneal rings following systemic immunisation

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From the Wills Eye Research Institute, Philadelphia, Pennsylvania, USA

SUMMARY Rabbits were hyperimmunised systemically over a 4-week period with bovine serum albumin (BSA) in complete Freund's adjuvants and were subsequently challenged systemically with a massive dose of BSA designed to produce serum sickness. Without any ocular manipulation a spontaneous corneal immune reaction was observed which we termed a 'reverse Wessely phenomenon'. It was due to a reversed sequence of antibody becoming sequestered in the cornea and later responding to antigen entering via the limbal circulation. In the stroma, lymphocytes were prominent and only few polymorphonuclear cells were found, but this may have been due to late sectioning of the corneas tested. The corneal ring formed at the limbus and migrated centripetally ahead of peripheral clouding, which is typical of the Wessely phenomenon. Possible relationships of this reaction with some autoimmune disorders are discussed.

Since the time when Wessely (1911) first demonstrated an immune reaction to foreign serum protein introduced into the rabbit cornea several other related immune phenomena have been described. Morawiecki (1956) demonstrated that the cornea could behave much like an agar substrate for migration of immune reactants in producing precipitin arcs as in gel diffusion. Parks *et al.* (1962) revealed a delayed hypersensitivity response in the cornea if it was overloaded with antigen in attempts to produce the Wessely phenomenon. The cornea was used for many years as the critical *in-vivo* test for delayed hypersensitivity to a given antigen (Salvin and Gregg, 1961). Sery *et al.* (1962, 1971) and Sery and Nagy (1971) showed that after recovering from an initial antigen sensitisation the cornea possessed an immune memory, independent of humoral immune factors, expressed as a local immune phenomenon for as long as 1 year after challenge. The same effect, described as 'super rings' by Breebaart and James-Witte (1959), was thought to be merely an amplified Wessely phenomenon, but the antigen diffusion kinetics and other characteristics were shown to be distinct (Sery and Nagy, 1962).

The Wessely phenomenon may be considered to be a type of Arthus phenomenon lacking only the characteristics of focal necrosis, but this is essentially a problem in terminology. The Arthus reaction depends on the presence, or close proximity, of blood capillaries which, on becoming clogged with immune precipitates and neutrophils, deprive the local tissue of nutrients. These vessels are lacking in the normal cornea. Thus attempts by Waksman and Bullington (1956) to demonstrate a passive Arthus reaction in the cornea failed for anatomical reasons. However, immune ring precipitates followed by influx of polymorphonuclear leucocytes which initiate the Arthus reaction in vascularised tissues do occur in the cornea (Waksman and Bullington, 1956; Salvin and Gregg, 1961; Sery *et al.*, 1962; Rahi and Tripathi, 1976).

The present study demonstrates another expression of the Wessely phenomenon which can be best explained as a 'reverse Wessely phenomenon', because antibody becomes sequestered in the cornea from the circulation during *systemic* immunisation and is manifested at a later time by systemic injection of a very large dose of that antigen. Thus, the immune precipitin reaction of the Wessely is reversed in the order which the immune reactants enter the cornea. Because this response is spontaneous in the normal cornea, which receives no direct manipulation, it may be comparable to corneal rings occasionally seen in patients with autoimmune disease with soluble immune complexes entering the cornea.

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Methods

Thirty-four 2·5-kg New Zealand white or chinchilla rabbits of both sexes were employed in these studies. They were sensitised intradermally on the back to bovine serum albumin (BSA, Sigma Chemical Co., St. Louis, Mo.) 1 mg/0·1 ml mixed with an equal volume of complete Freund's adjuvant on days 0, 7, and 14.

On day 21 the rabbits were challenged intraperitoneally with 250 mg of BSA (as a sterile 35% solution). Rabbits that did not develop corneal opacities within 2 weeks were rechallenged intravenously on days 41 and 112 with 250 mg of BSA.

Before sensitisation rabbit corneas were examined by biomicroscopy and transillumination and shown to be free of opacities and patent vessels. After challenge rabbits were examined daily during the first week, then every other day for the second week, and twice weekly thereafter.

Rabbit serum antibody was estimated by passive haemagglutination of sheep red blood cells conjugated to BSA with glutaraldehyde (Avrameas *et al.*, 1969). Titres were recorded as $\log_2$.

Rabbits were killed by an overdose of pentobarbitone and the eyes fixed in buffered formalin. Paraffin sections were stained with haematoxylin and eosine.

Various unfixed tissues of the eye were tested for the presence of antibody after extraction. Corneas were removed with a trephine to within 2 mm of the limbus. Each cornea (60 to 70 mg wet weight) was ground in a mortar with 1 g of silica and 10 volumes of saline. After storage at 4°C overnight, the mixture was centrifuged and the antibody in the supernatant estimated by passive haemagglutination. In a similar manner lenses were extracted with 4 volumes of saline for antibody determinations.

Results

RING FORMATION

During the sensitisation period no eye changes were observed. After the first antigen challenge (250 mg BSA intraperitoneally) 12 corneas in 9 rabbits developed corneal rings (Table 1). The earliest immune rings were seen 2 days after antigen challenge (Fig. 1). While the latest response occurred 13 days after challenge, the median response was seen by day 4. Corneal rings were first visible as a diffuse peripheral haze, randomly located along approximately one-third of the limbal margin. By the next morning a fine white arc was discernible. A white translucent area could be seen between the arc and the limbus. Gradually over a period of 1 to 2 days the arcs coalesced into rings as they migrated towards the centre of the cornea. The translucent area continued to occupy the area between the corneal rings and the limbus. After 1 week faint corneal rings continued, but the haze had cleared. Within 2 weeks the corneal ring had also cleared (Fig. 2). Not all eyes developed complete rings. Many formed arcs of from 90° up to 270°.

Table 1 *Incidence of reverse Wessely phenomenon with method and number of challenge*

	Challenge number			
	1st	*2nd*	*3rd*	*Total*
Intraperitoneal	12/42*	2/2	0/0	14/44
Intravenous	1/4	4/12	5/8	10/24
Total	13/46	6/14	5/8	24†/68

*Number of corneas developing ring arcs per total corneas in experimental group. †24 corneas in 16 rabbits

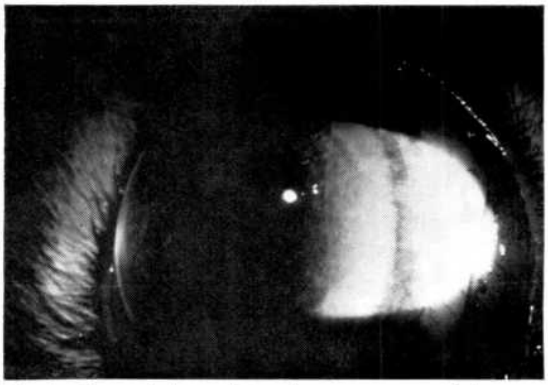

Fig. 1 *Corneal ring and translucent area seen 2 days after antigen challenge*

One rabbit received a 250-mg intraperitoneal antigen challenge of fluorescein-conjugated BSA on day 21, and the next day had a fluorescent line at the limbus of the left eye. By the second day green fluorescent arcs were detected with long wavelength ultraviolet light in both eyes, but the arcs were not visible by transillumination with white light.

ANTIBODY DETECTION

After 3 weekly antigen sensitisations specific antibody could be detected in cornea, aqueous humour, and serum but not in lens or vitreous humour (Table 2). While the amount of antibody in most of the corneas was 6 twofold dilutions lower (i.e., 1:64), corneal and serum titres were almost identical in 1 rabbit (No. 3193, Table 2). The variation in antibody titre for 2 rabbits developing rings during the course of the experiment is shown in Fig. 3.

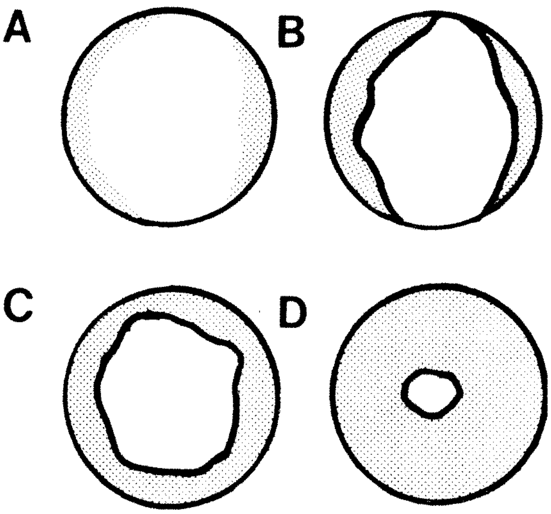

Fig. 2 *Diagrammatic development of reverse Wessely corneal rings. (A) Initial peripheral haze. (B) Fine white corneal arcs preceding translucent haze to centre of cornea. (C) Arcs coalesce to form a continuous corneal ring with translucent area to limbus. (D) Translucent area fades, leaving faint white ring which can still be discerned after 1 week*

Table 2 *BSA antibodies in ocular tissues and serum*

	Passive haemagglutination titre (log$_2$)									
Rabbit no.	*3185*		*3193*		*3212*		*3214*		*3216*	
Eye	*OD*	*OS*	*OD*	*OS*	*OD*	*OS*	*OD*	*OS*	*OD*	*OS*
Cornea*	8·3	8·3	7·8	6·9	5·3	5·3	5·3	7·3	6·3	<4·3
Aqueous	—	—	—	—	3·0	3·0	5·0	5·0	4·0	4·0
Lens†	—	—	—	—	<1·0	<1·0	<1·0	<1·0	<1·0	<1·0
Vitreous	—	—	—	—	2·0	1·0	<1·0	2·0	2·0	1·0
Serum‡	14·0		8·0		11·0		13·0		12·0	
Killed	D43		D43		D22		D22		D22	

*Corneas diluted 10-fold during homogenisation, except 3216 OS, which was diluted 20-fold. †Lenses diluted 4-fold during homogenisation. ‡Rabbits sensitised on day 0, 7, and 14, and serum obtained on the day killed (day 21)

HISTOLOGY

An extensive cellular infiltrate was found in the limbal region correlating with the clinical picture of rabbits having rings for several days. Infiltration up to 3 mm was occasionally seen, but no discrete histological process was seen at the demarcation of the corneal ring. The cellular infiltrate was composed of mononuclear leucocytes, which were predominantly lymphocytes. Occasional immature plasma cells and histiocytes were seen in the corneal stroma. Neutrophils were rarely seen in the corneal stroma, but small numbers could be found in the limbal region (Fig. 4).

Discussion

The Wessely phenomenon, or immune corneal rings, is the result of systemically formed antibody diffusing into a cornea containing residual *antigen* from a previous injection. We have referred to the study described in this report as the 'reverse' Wessely phenomenon, because we believe the antigen or a soluble immune complex of the antigen diffuses into a physiologically *antibody*-sensitised cornea.

Both models have several common properties. The corneal manifestations were almost identical, with initial peripheral corneal haze leading to sharply demarcated arcs or rings which migrate towards the centre of the cornea. Histologically, cellular infiltrates were an important facet of both phenomena. However, while the predominant infiltrative cell in the Wessely phenomenon is the neutrophil, there was a predominance of lymphocytes in the reverse Wessely phenomenon. Finding only rare neutrophils in the cornea during the active phase of ring formation and migration in the reverse Wessely phenomenon is probably the result of killing the animal after the neutrophil phase of ring formation had passed. A major difference between the 2 models lies in the production of immune corneal rings in the reverse Wessely phenomenon, *without* intraocular injection.

There are at least two possible mechanisms for the development of immune rings following the serum-sickness-induced reverse Wessely phenomenon.

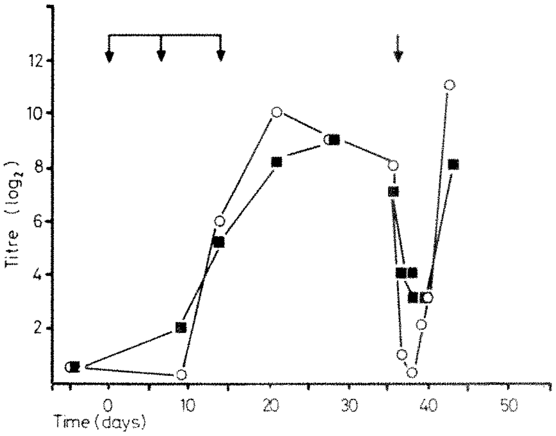

Fig. 3 *Antibody titres in 2 rabbits developing immune corneal rings. Antigen sensitisation on days 0, 7, and 14 (first 3 arrows). Intravenous antigen challenge on day 36 (last arrow) with 250 mg of BSA*

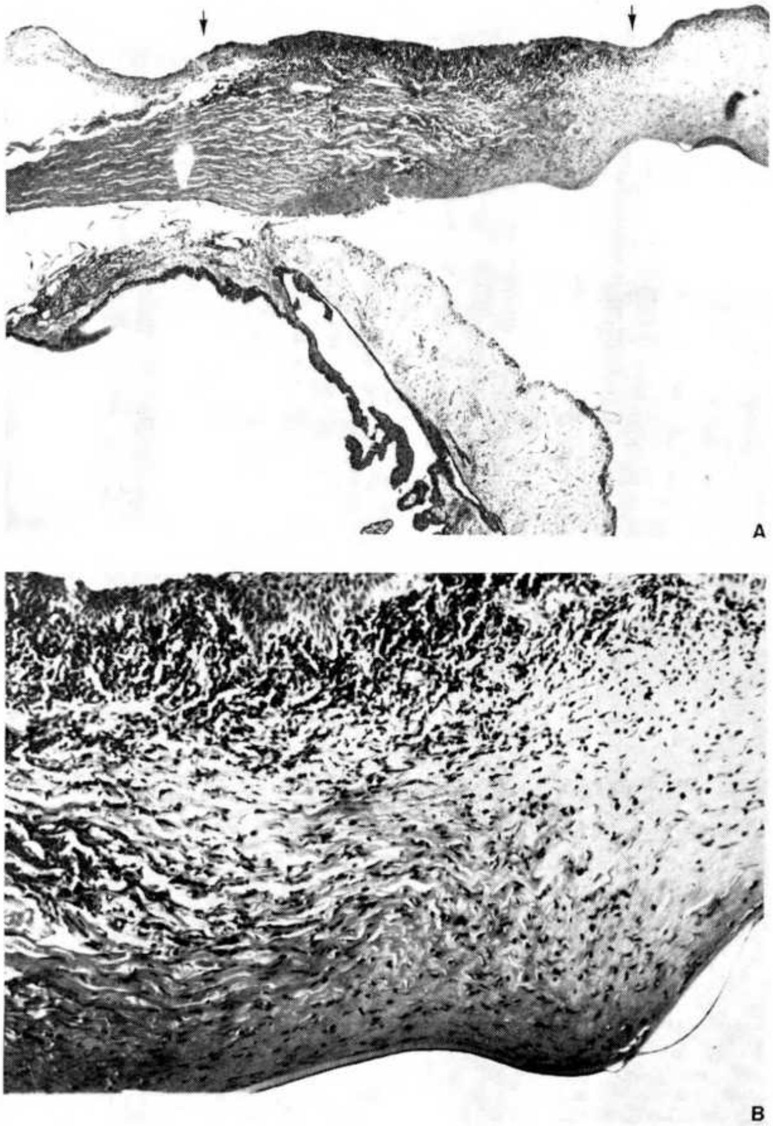

Fig. 4 *Cellular infiltrate in the cornea of the rabbit shown in Fig. 1. (A) Mononuclear leucocyte infiltrate in the cornea (between arrows) extending approximately 2·5 mm from the limbus. H. and E., original magnification* × 10. *(B) The lymphocyte is the predominant cell in the infiltrate. Occasional neutrophils were also seen in the cornea of this 4-day-old response. H. and E., original magnification* × 40

Immunoglobulin has been reported to be normally present in the cornea in a uniform concentration throughout the cornea (Allansmith *et al.*, 1971). Specific antibody was repeatedly detected in the cornea of sensitised rabbits at considerable titres (Table 2). Firstly, soluble immune complexes or unbound antigen may enter the cornea through limbal circulation or the anterior chamber and be rendered insoluble by the sequestered antibody. The immune precipitates are followed by cellular influx and the model is complete. A severe immunogenic uveitis usually accompanies serum sickness (Wong *et al.*, 1971; Friedman, 1976). Antibodies can enter the cornea from the anterior chamber and form immune precipitates in the cornea (Rahi and Tripathi, 1976). Alternatively a second mechanism can be proposed independent of the presence of specific antibody in the cornea. Rahi and Garner (1976) suggest that immune complexes persist at the limbus because of the absence of corneal circulation. The influx and activation of complement at the limbus might change the permeability of the limbal vessels, allowing the rapid influx of leucocytes, giving rise to the corneal rings. At present neither mechanism is favoured over the other, and each may play a part in immune ring development.

The variability in the production of the reverse Wessely immune rings may be due to the variability in the development of serum sickness. For example, 2 rabbits not reported in this study were initially sensitised and challenged with antigen but died from serum sickness within several hours. Other rabbits in the study showed little or no uveitis, a finding suggesting reduced development of serum sickness. Serial antibody titres were not determined in all rabbits as described in Fig. 3, nor were complement levels measured, so that the degree of serum sickness in each animal was not known.

Several human autoimmune diseases have rare corneal manifestations such as marginal furrowing ulceration and peripheral opacification (Rahi and Garner, 1976; Ginsberg, 1976). It is possible that these corneal changes may occur by a mechanism similar to the reverse Wessely phenomenon. It is suggested that circulating immune complexes arrive at the limbus and remain because of a lack of corneal vascularisation. Activation of complement by the immune complex may trigger cellular infiltration, resulting in the appearance of immune rings.

In the serum-sickness-induced reverse Wessely phenomenon the cornea clears within 2 weeks, leaving no clinical evidence of opacification. In human immune complex disease, such as rheumatoid arthritis, polyarteritis nodosa, systemic lupus erythematosus, and relapsing polychondritis, occasional peripheral corneal opacification and ischaemic necrosis can be found (Rahi and Garner, 1976; Ginsberg, 1976). Continuous deposition of immune complexes at the limbus, along with C′-mediated local tissue destruction and neutrophil infiltration, may be responsible for the marginal ulceration or ischaemic necrosis seen on occasion in patients with these autoimmune diseases.

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References

Allansmith, M., Newman, L., and Whitney, C. (1971). The distribution of immunoglobulin in the rabbit eye. *Archives of Ophthalmology*, **86**, 60–64.

Avrameas, S., Taundon, B., and Chuilon, S. (1969). Glutaraldehyde, cyanuric chloride and tetraazotized O-dianisidine as coupling reagents in the passive hemagglutination test. *Immunochemistry*, **6**, 67–76.

Breebaart, A. C., and James-Witte, J. (1959). Studies on experimental corneal allergy. *American Journal of Ophthalmology*, **48**, 37–47.

Friedman, A. H. (1976). Ocular hypersensitivity. In *Clinical Ophthalmology*, vol. 5, chapter 28. Edited by T. D. Duane. Harper and Row: Hagerstown.

Ginsberg, S. P. (1976). Corneal problems in systemic disease. In *Clinical Ophthalmology*, vol. 5, chapter 43. Edited by T. D. Duane. Harper and Row: Hagerstown.

Morawiecki, J. (1956). Präzipitationserscheinungen in der lebenden Hornhaut bei Antigen-Antikorperraktionen. *Ophthalmologica*, **132**, 236–243.

Parks, J. J., Leibowitz, H. M. L., and Maumenee, A. E. (1962). A transient stage of suspected delayed sensitivity during the early induction phase of immediate corneal sensitivity. *Journal of Experimental Medicine*, **115**, 867–880.

Rahi, A. H. S., and Garner, A. (1976). *Immunopathology of the Eye*, p. 131. Blackwell: Oxford.

Rahi, A. H. S., and Tripathi, R. C. (1976). Anatomy of passive arthus reaction in the cornea. *Modern Problems in Ophthalmology*, **16**, 155–160.

Salvin, S. B., and Gregg, M. B. (1961). The specificity of allergic reaction. 4. The cornea. *Proceedings of the Society for Experimental Biology and Medicine*, **107**, 478–483.

Sery, T. W., Pinkes, A. H., and Nagy, R. M. (1962). Immune corneal rings. 1. Evaluation of reactions to equine albumin. *Investigative Ophthalmology*, **1**, 672–685.

Sery, T. W., and Nagy, R. M. (1962). Immune corneal rings. 3. Mechanism of local immune corneal ring formation. *Investigative Ophthalmology*, **1**, 762–772.

Sery, T. W., Nagy, R. M., and Barber, G. W. (1971). Corneal hypersensitivity. 1. Escape kinetics of antigen from sensitized corneas. *Journal of Immunology*, **106**, 217–222.

Sery, T. W., and Nagy, R. M. (1971). Corneal hypersensitivity. 2. Specific binding of antigen in sensitized corneas. *Journal of Immunology*, **106**, 226–232.

Waksman, B. H., and Bullington, S. J. (1956). A quantitative study of the passive Arthus reactions in the rabbit eye. *Journal of Immunology*, **76**, 441–453.

Wessely, K. (1911). Ueber anaphylaktische Erscheinungen an der Hornhaut (experimentelle Erzeugung einer parenchymatosen Keratitis durch artfremdes Serum). *Münchener medizinische Wochenschrift*, **58**, No. 32.

Wong, V. G., Anderson, R. R., and McMaster, P. R. B. (1971). Endogenous immune uveitis. The role of serum sickness. *Archives of Ophthalmology*, **85**, 93–102.

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Adenovirus type 21 keratoconjunctivitis

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SUMMARY A case of keratoconjunctivitis caused by adenovirus type 21 in London has been described. A 59-year-old woman attended hospital in August 1974 complaining of a 3-week history of redness, grittiness, watery discharge, and photophobia in her left eye and a slight upper respiratory infection. Clinical examination showed a moderate follicular conjunctivitis mainly in the lower and upper fornices, which lasted for 6 weeks. In the cornea a moderate amount of epithelial and subepithelial punctate keratitis was observed. The subepithelial opacities were coarse, discrete, and round and lasted for 4 months. The course of follicular conjunctivitis and the subepithelial punctate keratitis in this patient was similar to epidemic keratoconjunctivitis caused by adenovirus 8. A conjunctival swabbing collected from this patient was positive for adenovirus serotype 21.

Adenovirus types 2, 3, 4, 5, 7, 8, 11, 13, 14, 15, and 19 have been isolated from the eyes of patients suffering from keratoconjunctivitis (Editorial, 1977). Adenovirus types 3 and 7 are the commonest causes of sporadic keratoconjunctivitis, and adenovirus 8 is generally associated with outbreaks of epidemic keratoconjunctivitis. Adenovirus 19 in recent years has been responsible for sporadic cases as well as the outbreaks of keratoconjunctivitis resembling epidemic keratoconjunctivitis in several countries (Hierholzer *et al.*, 1974; Darougar *et al.*, 1977).

Adenovirus 21 was first isolated from a Saudi Arabian patient with signs of trachoma (Bell *et al.*, 1960). Subsequently the agent was isolated in Holland, India, and the United Kingdom from patients suffering from respiratory infections (McDonald *et al.*, 1962; Kurian *et al.*, 1962; Pereira, 1963). Follicular conjunctivitis caused by adenovirus 21 has been reported in a family in Italy (Piazza and Paradisi, 1968).

This paper reports a case of follicular conjunctivitis with subepithelial punctate keratitis caused by adenovirus 21 in London. This is the first report of adenovirus 21 keratoconjunctivitis in the United Kingdom.

Case history

A 59-year-old married woman attended the External Eye Diseases Clinic of Moorfields Eye Hospital in August 1974 complaining of redness, grittiness, watering, discharge, and photophobia in her left eye for 3 weeks. She had a slight upper respiratory infection with coughing that had begun just before the conjunctivitis. There was no known contact with ocular or respiratory infection. One year earlier this patient had had a mild papillary conjunctivitis with watering and grittiness.

The unaided visual acuity was 6/18 in both eyes. There was slight ptosis in the left eye and the bulbar conjunctiva was slightly hyperaemic. Slit-lamp examination of the left eye showed moderate palpebral papillary hyperplasia, especially in the upper tarsal conjunctiva, and a moderate follicular hypertrophy with small, discrete, and gelatinous follicles mainly in the upper and lower fornices. The cornea showed moderate epithelial and subepithelial punctate keratitis in the interpalpebral area. The subepithelial opacities (10 to 15) were coarse, discrete, and round with regular margins. Some of these opacities were visible with the naked eye. No abnormality was observed in the uveal tract or fundus of this eye. The right eye was normal except for a few papillae and old follicles. Treatment with chloramphenicol eye drops 5 times daily, which had been prescribed by her family doctor, was continued.

Three weeks later (6 weeks from the onset) she was asymptomatic. There was no abnormality in the lids, bulbar conjunctiva, or palpebral conjunctiva, except for a few papillae and old follicles. The

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subepithelial punctate keratitis was still present. Three months later (18 weeks from the onset) the keratitis had completely resolved.

Swabs from the conjunctiva of the left eye were collected 3 weeks after the onset of the infection and were inoculated into 2 tubes of embryonic kidney cells (HEK) (McSwiggan *et al.*, 1975). The first cytopathic effect (CPE) appeared towards the end of the second week. The second and third passage of the virus in HEp2 cells produced CPE in less than 4 days. Adenovirus 21 was identified by the standard neutralisation test. The complement fixation test on blood samples collected 3 weeks and 6 weeks after the onset showed a steady titre of 1/40 against adenovirus group antigen.

Discussion

Adenovirus 21 was associated with outbreaks of respiratory infection among military recruits in Holland and India (McDonald *et al.*, 1962; Kurian *et al.*, 1962). In the United Kingdom the virus has been isolated from patients of all ages, causing severe respiratory disease among infants and a milder disease in older patients (Pereira, 1963). The isolation of adenovirus 21 from the stools of apparently normal children and the detection of specific antibodies in the sera of adults (Pereira, 1963) suggests that the virus has been prevalent in the United Kingdom.

Ocular infection with adenovirus 21 has not been reported since the original isolation in Saudi Arabia in 1960 except in a family in Italy (Piazza and Paradisi, 1968). Six children belonging to that family developed unilateral or bilateral follicular conjunctivitis without keratitis which lasted for 2 weeks. The eye infection was accompanied by pharyngitis, nasal congestion, and general malaise. No ocular or respiratory infection was observed in the parents.

In the case of our patient there was no evidence of ocular or respiratory infection in her family or contacts, nor was there any evidence of major ocular viral outbreaks in London at that time. The moderate follicular conjunctivitis recorded in this patient was observed 3 weeks after the onset of her infection and may have been preceded by more severe inflammation. However, the long course of conjunctivitis (6 weeks), the low-grade associated upper respiratory infection, and the type, as well as the size, of subepithelial punctate keratitis were similar to the keratoconjunctivitis caused by adenovirus 8 or 19 (Jones 1962; Darougar *et al.*, 1977). The isolation of adenovirus 21 from the eye indicates that adenovirus 21, which is prevalent in the United Kingdom and commonly isolated from stools (Pereira, 1963), may be a potential cause of sporadic cases or institutional outbreaks of keratoconjunctivitis.

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References

Bell, S. D., Jr., Rota, T. R., and McComb, D. E. (1960). Adenovirus isolated from Saudi Arabia—six new serotypes. *American Journal of Tropical Medicine and Hygiene*, **9**, 523–526.

Darougar, S., Quinlan, M. P., Gibson, J. A., Jones, B. R., and McSwiggan, D. A. (1977). Epidemic keratoconjunctivitis and chronic papillary conjunctivitis in London due to adenovirus type 19. *British Journal of Ophthalmology*, **61**, 76–85.

Editorial (1977). Adenovirus keratoconjunctivitis, *British Journal of Ophthalmology*, **61**, 73–75.

Hierholzer, J. C., Guyer, B., O'Day, D. M., and Shaffner, W. (1974). Adenovirus type 19 keratoconjunctivitis. *New England Journal of Medicine*, **290**, 1436.

Jones, B. R. (1962). Adenovirus infections of the eye in London. *Transactions of the Ophthalmological Societies of the United Kingdom*, **82**, 621–640.

Kurian, P. V., Mukundan, P., and Karpagaganapathy, P. (1962). Isolation of adenovirus type 21. *Lancet*, **2**, 355.

McDonald, J. C., Miller, D. L., Zuckerman, A. J., and Pereira, M. S. (1962). Coe (coxsackie) virus, para-influenza virus and other respiratory infections in the R.A.F., 1958–1960. *Journal of Hygiene*, **60**, 235–248.

McSwiggan, D. A., Darougar, S., Rahman, A. F. M. S., and Gibson, J. A. (1975). Comparison of the sensitivity of human embryo kidney cells, HeLa cells, and W138 cells for the primary isolation of viruses from the eye. *Journal of Clinical Pathology*, **28**, 410–413.

Pereira, M. S. (1963). Occurrence of adenovirus type 21 in Great Britain. *British Medical Journal*, **1**, 728–729.

Piazza, M., and Paradisi, F. (1968). Episodo familiare di infeziore da adenovirus tipo 21 (congiunitivite follicolare). *Rivista dell'Instituto Sieroterapico Italiano*, **43**, 241–243.

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Scanning electron microscope study of herpes simplex virus experimental disciform keratitis

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SUMMARY Scanning electron microscopy of the endothelium of experimental disciform keratitis revealed corneal endothelial changes which distinguished disciform oedema from the more progressive stages of disciform keratitis. The endothelium of corneas with disciform oedema were wholly intact and characterised by subtle morphological alterations. In contrast, the more progressive stages of disciform keratitis were characterised by massive destruction and denudation of the endothelium. The significance of these observations is discussed.

The exact aetiology of disciform oedema, a discrete stage of disciform keratitis, remains unknown. Clinical specimens obtained from candidates for corneal transplant show chronic deep stromal herpes disease (Dawson *et al.*, 1968). Disciform keratitis is induced in animals by severe corneal infections, hyperimmunisation procedures, or both (Williams *et al.*, 1965; Swyers *et al.*, 1967; Meyers and Pettit, 1973; Hoffman *et al.*, 1976). As a result clinical and experimental specimens include a variety of immunological and infectious complications. It has been reported that the endothelium of these corneas shows several morphological changes. These alterations may include cellular oedema, giant cell formation, derangement of cells, distinct viral plaques, peripheral endothelial denudation, and more pronounced central endothelial damage (Hogan *et al.*, 1963; Irvine and Kimura, 1967; Oh, 1970).

The experimental disciform keratitis model described by Sery *et al.* (1972) was used throughout this study. This unique model permits separation of discrete disciform oedema from the more progressive stages of the disease. The purpose of this scanning electron microscopic (SEM) investigation was to observe the endothelial topography of corneas during the discrete stage of disciform oedema. As a comparison corneal specimens from eyes with more progressive stages of disciform keratitis as well as injured uninfected controls were observed.

Materials and methods

Virus propagation. Rabbit corneal fibroblast cultures established in our laboratory were grown in Eagle's minimal essential medium (MEM) supplemented with 10% heat-inactivated foetal calf serum and antibiotics. When confluent, the monolayer cultures were washed 3 times with phosphate buffered saline (pH 7·2) to eliminate most of the foetal calf serum. The cultures were then seeded with the H-4 strain of herpes simplex virus at a multiplicity of infection of 4 to 7 virus particles per cell. Medium 199 without serum was added for virus propagation. After 40 hours of incubation at 34°C the virus suspensions were harvested, titered, and diluted in Medium 199 to a final concentration of 10 000 virus particles per millilitre.

Animal inoculation. Normal grey chinchilla rabbits weighing 2 to 2·5 kg were used in this study. The corneas were anaesthetised by topical administration of 1% proparacaine hydrochloride (Ophthaine). Both eyes of 10 test animals received intrastromal injections of 200 H-4 virus particles in 0·02 ml of Medium 199, while both eyes of 5 control rabbits received an intrastromal injection of 0·02 ml of Medium 199 only.

Preparation of whole corneas for SEM. Slit-lamp examination of virus-inoculated corneas verified the presence of disciform keratitis. Within 1 to 2 days after the occurrence of disease the rabbits were killed with an overdose of sodium pentobarbital. In addition control rabbits were killed at various times. After enucleation all corneas were excised, leaving a 1-mm scleral ring, and fixed for 3 hours in

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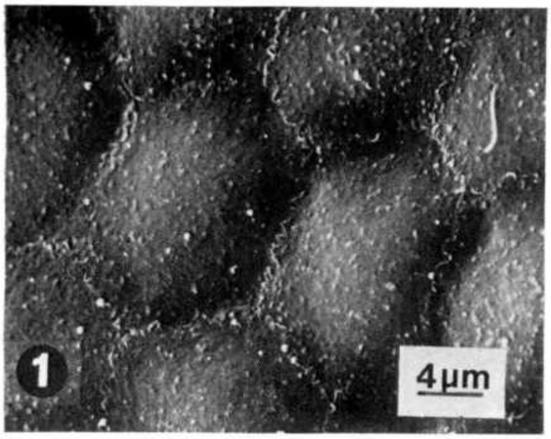

Fig. 1 *Normal mosaic-like pattern of rabbit corneal endothelium. Cell borders are well defined, while small finger-like microvilli are evenly distributed over the cell surfaces* (× *1900*)

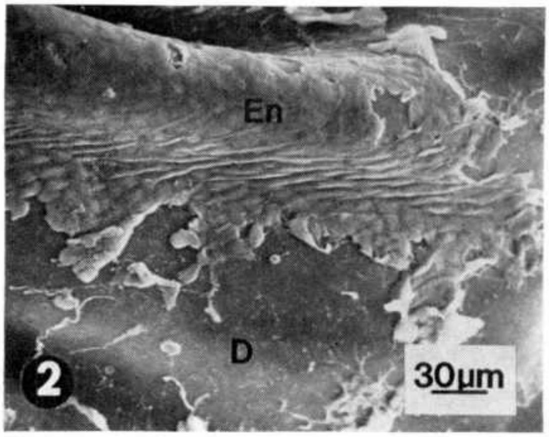

Fig. 2 *Endothelium (EN) of a rabbit cornea which presented with a dendritic lesion and disciform oedema is denuded, exposing large areas of Descemet's membrane (D)*

cold (4°C) 2·7% glutaraldehyde buffered to pH 7·2 with 0·2 M sodium cacodylate-HCl.

After primary fixation the corneas were washed twice in cacodylate-HCl buffer, post-fixed for 1 hour in cold (4°C) 0·5% osmium tetroxide buffered to pH 7·2 with 0·2 M cacodylate-HCl, and washed twice in buffer for 2 15-minute intervals. The corneas were then dehydrated at 15-minute intervals in graded ethanol (30, 50, 70, 90, 100%), ethanol-amyl acetate (50/50%), and amyl acetate (100%). While submerged in amyl acetate the specimens were processed through a Sorvall critical point drying apparatus using CO_2 according to the technique described by Anderson (1951). After drying the corneas were mounted (endothelial side up) on stubs, coated with carbon and gold, and examined at 25 kV in a Joel JSM 50-A scanning electron microscope with the specimen tilted at 30°.

Results

Rabbit corneas injected intrastromally with a low dose of the highly invasive H-4 strain of herpes simplex virus present a classical disciform keratatis

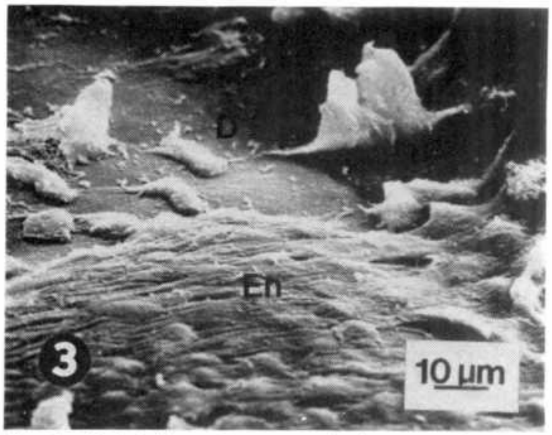

Fig. 3 *Endothelium of a cornea which presented with benign disciform keratitis showed large areas of peripheral denudation with exposure of Descemet's membrane (D). The endothelium (EN), which remained intact, appears abnormal* (× *630*)

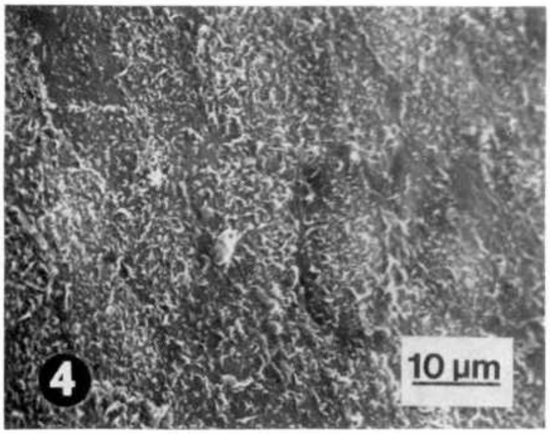

Fig. 4 *The endothelium of a cornea which presented with a small dendritic lesion and subsequent disciform oedema showed this centrally located area of irregular topography. When compared to normal endothelium (Fig. 1) cell surfaces appear active, with an exaggerated number of microvilli. In addition, cell borders are ill defined* (× *1000*)

with or without complicating dendritic keratitis. This experimental disease displays features similar to the clinical syndrome described in man. In its most benign form symptoms of the experimental disciform keratitis include stromal oedema and haze, while moderate stages show diffuse oedema, granular infiltrates, and anterior uveitis. In benign and moderate disease the epithelium generally remains intact. In the more severe form of the disease stromal necrosis, neovascularisation, and surface epithelial lesions are evident.

The corneal endothelium from 3 groups of rabbits was evaluated for topographical changes. The first group of animals included those which received an instrastromal injection of virus and, when killed, displayed disciform keratitis as well as small surface dendritic lesions. The second group of rabbits received an intrastromal injection of virus but, when killed, displayed disciform oedema with no prior episode of dendritic keratitis. Finally, the third group of rabbits received an intrastromal injection of Medium 199, and therefore served as non-infected, traumatised controls.

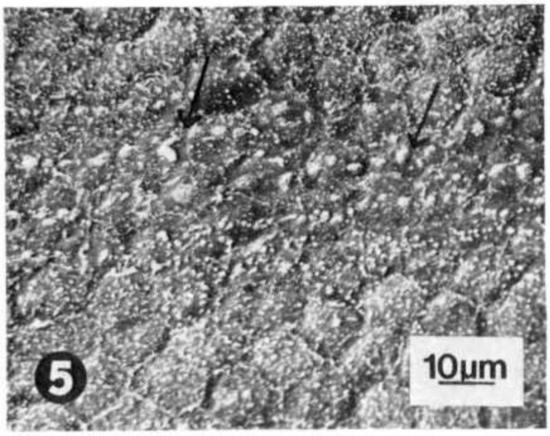

Fig. 5 *The endothelium of a cornea with benign disciform keratitis showed a subtle area of abnormal topography observed as a line (arrows) in the centre of this micrograph* (× *630*)

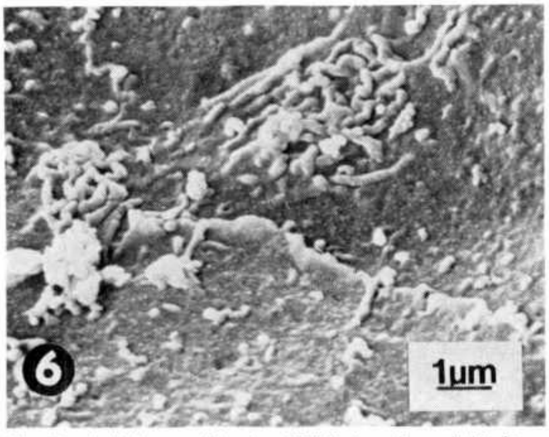

Fig. 6 *A high-magnification SEM view showed this line to be formed by the aggregation or agglutination of microvilli* (× *6300*)

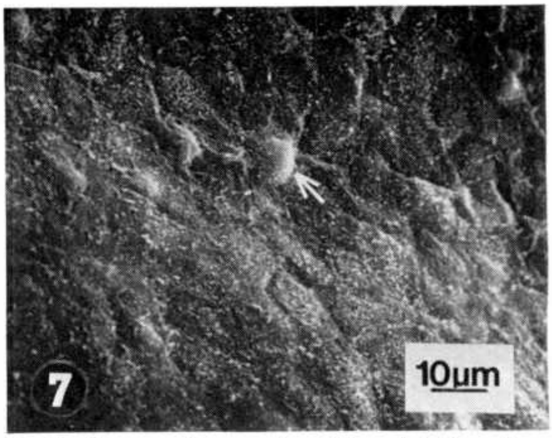

Fig. 7 *The normal topography of the endothelium of a cornea which presented with benign disciform keratitis is interrupted by irregularly shaped and enlarged cells (arrow)* (× *630*)

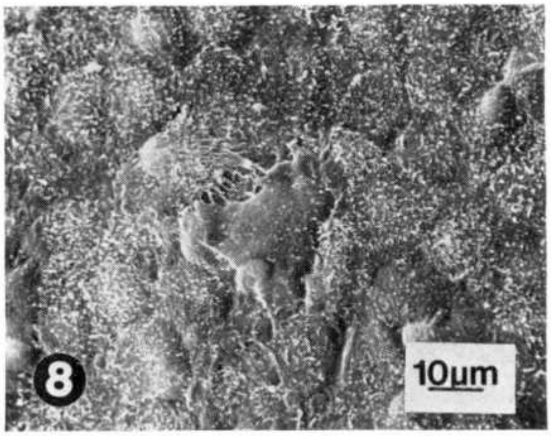

Fig. 8 *In addition the same cornea (Fig. 7) showed endothelial 'giant' cell formation as observed in the centre of this photomicrograph. An increased number of microvilli is also evident* (× *630*)

All corneas from the control group showed the normal mosaic-like pattern of endothelium (Fig. 1). Cell borders were well defined, and relatively few microvilli were evenly distributed over the smooth surfaces of the cells.

With rabbits displaying progressive stages of

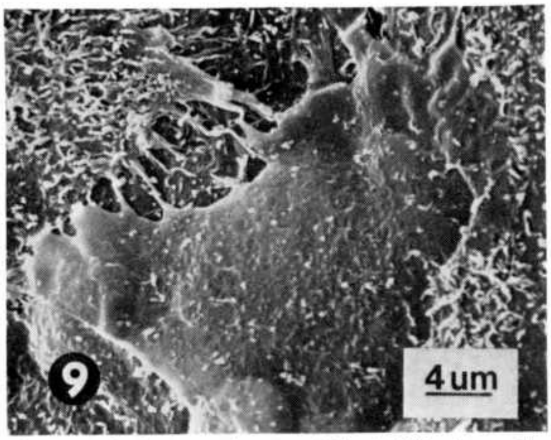

Fig. 9 *A higher magnification of Fig. 8. This giant cell is either a single oedematous cell or the fusion of cells. Multinuclear giant cells are observed in herpes virus infected corneal fibroblasts* in vitro (× *1900*)

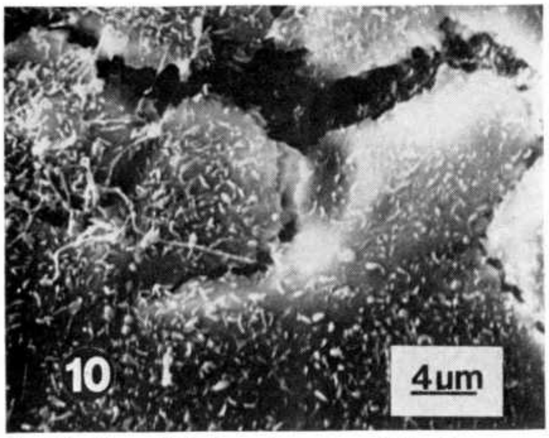

Fig. 10 *The endothelium of a cornea with benign disciform keratitis showed these large irregular cells. The junctions between these cells have broken down* (× *1900*)

disciform keratitis (those corneas showing concurrent small dendritic lesions) massive destruction and denudation of the endothelium was evident (Fig. 2). Endothelial damage within this group was generally confined to the periphery (Fig. 3). However, we were able to correlate the severity of anterior uveitis with progressive central endothelial damage. Although some areas of the endothelium remained intact, certain morphological alterations were evident. These included loss of defined cell boundaries and more active cell surfaces expressed by the significant increase in the number and length of microvilli (Fig. 4). In addition to the morphological changes all endothelium within this group showed a large number of inflammatory cells at the limbus.

The endothelial alteration associated with benign disciform keratitis is more subtle. Wholly intact endothelium had cells with extraordinary surface activity in the form of increased number and the agglutination of microvilli (Figs. 5, 6). In addition cellular oedema (Fig. 7) with concomitant opening-up of intercellular junctions (Figs. 10, 11), and giant cell formation (Figs. 8, 9) was evident. Within this group 1 animal (both corneas) had endothelium

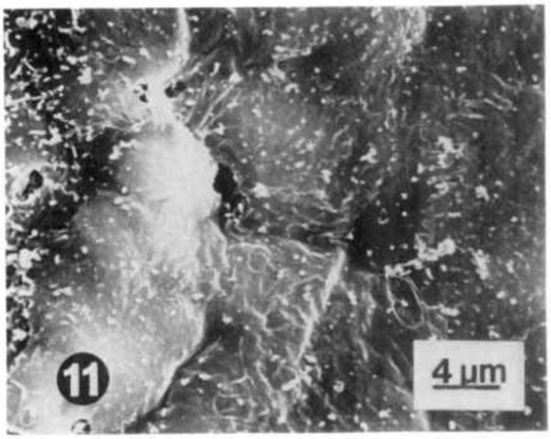

Fig. 11 *This photomicrograph of a benign disciform cornea shows oedematous, irregularly shaped endothelial cells. Cell borders are ill defined, while gaps appear between some of the cells* (× *1900*)

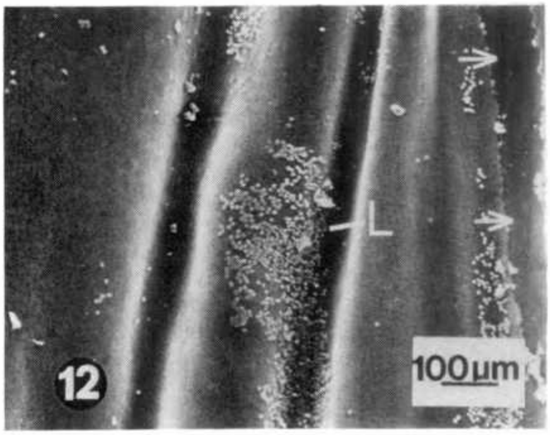

Fig. 12 *This photomicrograph of the endothelium of a cornea with benign disciform keratitis shows massive invasion of leucocytes (L). In addition large numbers of leucocytes were also observed at the limbus. The endothelium has remained intact except at the periphery, where large denuded areas expose Descemet's membrane (arrows)* (× *63*)

with peripheral denudation (Figs. 3, 12). In addition a massive influx of inflammatory cells was evident at the limbus (Fig. 12).

Discussion

SEM of the corneal endothelium from animals with experimental progressive disciform keratitis showed changes such as cellular oedema, cell derangement, and peripheral denudation. These observations confirm the findings of Irvine and Kimura (1967) and Oh (1970). In contrast we observed that peripheral denudation was accompanied by an influx of inflammatory cells. In addition we are able to correlate centralised endothelial damage with the severity of the disciform keratitis and anterior uveitis.

Our SEM study reveals that benign experimental disciform keratitis is characterised by an intact endothelium, which is modified by subtle and diffuse morphological changes. These changes correlate with the appearance of deep stromal corneal oedema. Oh (1970) described the relationship of deep corneal opacity and diffuse endothelial lesions after anterior chamber inoculation of HSV. He also observed distinct plaques of viral origin on the endothelium of corneas with or without opacities. In the present study distinct endothelial plaques are not apparent at any stage of HSV induced disciform keratitis. Moreover, we could not confirm the report by Irvine and Kimura (1967) that the central endothelium is most severely damaged beneath the area of stromal oedema.

Histological evaluation of the intrastromal low-dose virus model of disciform keratitis has shown the appearance of inflammatory cell types in diseased corneas (Sery and Nagy, 1977). Mononuclear leucocytes are the most consistently observed inflammatory cell type, while polymorphonuclear leucocytes may be scarce or absent. When draining lymph node cells are tested against specific HSV antigens via blast transformation assays, no significant response to specific HSV antigens is evident during the discrete stage of disciform oedema (Nagy *et al.*, 1975). However, as the severity of disciform keratitis increases, specific HSV induced lymphocyte blast transformation becomes evident.

These findings, in addition to the present investigation, suggest that the early stage of disciform keratitis may be composed of two distinct phases. The initial phase is non-specific; the corneal endothelium remains intact, but characteristic subtle and diffuse lesions are evident. Although leucocytes infiltrate the corneal stroma, inflammatory cells are noticeably absent from the anterior chamber. Regional draining lymph node cells tested at this time show no reactivity to specific HSV antigens. The second phase of early disciform keratitis is accompanied by an acute inflammatory reaction within the anterior chamber. Peripheral endothelial denudation is observed and may become more progressive toward the centre. This second phase is specific, that is, there is evidence of HSV antigen specific cell-mediated immunity by the lymphocytes of regional draining lymph nodes.

Endothelial destruction during disciform keratitis may be the result of direct viral invasion, lymphocyte-mediated cytotoxicity, or other immune mechanisms. Further investigations are at present under way to clarify the relative role of viral and immunological factors in the early stage of disciform keratitis.

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References

Anderson, T. F. (1951). Techniques for the preservation of three-dimensional structures in preparing specimens for electron microscopy. *Transactions of the New York Academy of Sciences*, **13**, 130–133.

Dawson, C., Togni, B., and Moore, T. E. (1968). Structural changes in chronic herpetic keratitis. *Archives of Ophthalmology*, **79**, 740–747.

Hoffman, F., Harnisch, J. P., Dumitrescu, L., Haase, J., and Museteanu, Cr. (1976). Herpes simplex corneae: a scanning and transmission electron microscopic study of the rabbit eye. In *The Structure of the Eye III*, pp. 77–86. Edited by Yamada and Mishima.

Hogan, M. J., Kimura, S. J., and Thygeson, P. (1963). Pathology of herpes simplex keratouveitis. *Transactions of the American Ophthalmological Society*, **61**, 75–99.

Irvine, A. R., and Kimura, S. J. (1967). Experimental stromal herpes simplex keratitis in rabbits. *Transactions of the American Ophthalmological Society*, **65**, 189–210.

Meyers, R. L., and Pettit, T. H. (1973). Corneal immune response to herpes simplex virus antigens. *Journal of Immunology*, **110**, 1575–1590.

Nagy, R. M., McFall, R., and Sery, T. W. (1975). The relationship of cell mediated immunity to a classical herpes simplex disciform keratitis. The Association for Research In Vision and Ophthalmology, Spring Meeting, Sarasota, Florida.

Oh, J. O. (1970). Endothelial lesions of rabbit cornea produced by herpes simplex virus. *Investigative Ophthalmology*, **9**, 196–205.

Sery, T. W., Nagy, R. M., and Nazario, R. (1972). Experimental disciform keratitis. 3. Virus infectivity versus hypersensitivity in herpesvirus stromal disease. *Ophthalmic Research*, **4**, 137–144.

Sery, T. W., and Nagy, R. M. (1977). Cellular reaction in experimental herpetic disciform keratitis. *American Journal of Ophthalmology*, **84**, 675–680.

Swyers, J. S., Lausch, R. N., and Kaufman, H. E. (1967). Corneal hypersensitivity to herpes simplex. *British Journal of Ophthalmology*, **51**, 843–846.

Williams, L. E., Nesburn, A. B., and Kaufman, H. E. (1965). Experimental induction of disciform keratitis. *Archives of Ophthalmology*, **73**, 112–114.

British Journal of Ophthalmology, 1978, 62, 843–849

Acute follicular conjunctivitis and keratoconjunctivitis due to herpes simplex virus in London

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SUMMARY During the 18 months January 1975 to June 1976, 25 cases of acute herpetic follicular conjunctivitis and keratoconjunctivitis resembling adenovirus ocular infection presented in the External Eye Disease Clinic, Moorfields Eye Hospital, City Road, London. Herpes simplex virus was isolated in HEp2 cells in 22 patients, and the remaining 3 patients were identified by a minimum 4-fold rise in the level of antiherpes simplex virus antibody in their blood. No adenovirus was isolated from these patients, but complement fixation test for adenovirus was positive in 1 patient with cultural test positive for herpes simplex virus. Most patients were between 20 and 35 years old and the ratio of males to females was 12 to 13. At the initial visit the clinical features of disease were moderate to severe conjunctival papillary and follicular reactions with epithelial and subepithelial punctate keratitis but little systemic disease. In the absence of typical herpetic lesions of face, lids, or cornea the disease resembled adenovirus types 8 or 19 keratoconjunctivitis. Of these 25 patients 5 subsequently developed typical herpetic lesions of lids or cornea. In the remaining 20 cases the correct diagnosis could be made only by cultural or serological tests. Virological diagnosis provides a rational basis for antiherpetic chemotherapy, which appears to shorten the course of infection.

Acute primary herpetic blepharokeratoconjunctivitis and chronic recurrent keratitis are common manifestations of herpes simplex virus (HSV) infection. Less well recognised is acute follicular conjunctivitis without characteristic lid or corneal lesions.

This report presents the findings in 25 cases of acute herpetic follicular conjunctivitis which presented without characteristic lid, face, or corneal signs of herpetic infections. In most of them, the correct diagnosis could be made only by cultural or serological tests for HSV infection.

Methods and patients

Patients with acute follicular conjunctivitis or keratoconjunctivitis without facial, lid, or corneal lesions typical of HSV infection at the first visit, but with positive cultural or serological tests for HSV, were included.

The patients were examined with a Haag-Streit slit lamp and symptoms were graded on a 0 to 3 scale (mild, moderate, severe) as described previously (Darougar *et al.*, 1977b). Conjunctival swabbings were placed in plastic capsules containing 2 SP transport medium (Gordon *et al.*, 1969) with 3% fetal bovine serum and stored in a refrigerator at –70°C. Each clinical specimen was inoculated into 2 tubes containing HEp2 cells. Cultures were maintained for 21 days and examined frequently for the presence of cytopathic effect (CPE) (McSwiggan *et al.*, 1975). Isolates were identified by the fluorescent antibody test.

Sera collected by venepuncture at intervals of 2 to 3 weeks were tested by a complement fixation test (CFT) for herpes simplex virus and adenovirus group antibodies. Conjunctival impressions taken from some patients by specially-designed plastic spatulae were fixed, stained, and examined by the method described by Thatcher *et al.* (1977).

Results

During the 18 months January 1975 to June 1976 25 patients with acute follicular conjunctivitis and

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no herpetic lesions of the lids, face, or cornea at the time of their first visit to the clinic, but with positive cultural or serological tests for herpes simplex virus, were identified. Of these 25 patients 5 subsequently developed palpebral vesicles or dendritic ulcers.

The patients' ages ranged from 8 to 50 years, the majority being between 20 and 35 years. The ratio of males to females was 12 to 13. Of these 25 cases 18 were diagnosed in 1975 and 7 in the first 6 months of 1976. No seasonal pattern of incidence was observed.

PREVIOUS HISTORY

Five patients gave a history of previous infection suggestive of herpes simplex: 3 had recurrent cold sores on nose or lips, 1 had lid disease (possibly herpetic) 5 years previously, and 1 had a history of a possible corneal ulcer 5 years previously. In no case was there a clear history of previous ocular herpetic infection.

Of the 25 patients 2 had been in contact with patients with cold sores, 3 in contact with other persons suffering from conjunctivitis, and a further 3 had been in swimming pools 9 to 21 days before the onset of their ocular infection. In 1 of this latter group some fellow swimmers had also developed conjunctivitis at the same time. In the other 17 cases there was no history of contact with other patients nor had they attended hospitals, clinics, or a swimming pool.

In 5 cases there was a history of pharyngitis and rhinitis during the week preceding the conjunctivitis. Another patient had a cold 3 weeks before developing eye disease. One patient had Hodgkin's disease and was on systemic treatment with prednisolone 5 mg daily.

SYMPTOMS AND SIGNS

Fifteen of the 25 patients had enlarged preauricular lymph nodes, which in 12 cases were tender. In 8 cases in which the disease affected both eyes the lymphadenopathy was bilateral.

The commonest symptoms were moderate hyperaemia associated with lacrimation, discharge, grittiness, and swelling of the lids (Table 1 and Fig. 1).

In 8 cases the second eye became inflamed in less than 1 week from the onset of the infection. In the other 17 the infection remained unilateral. The average duration of conjunctival inflammation was 4 weeks (range 2 to 12 weeks). In 17 cases lids showed diffuse oedema and mild to moderate erythema. No vesicle or ulceration was observed in these cases at the initial examination. However, in 4 cases vesicles or ulcers developed on the lid 2 to 3 days after the first examination.

The bulbar conjunctiva showed mild to moderate hyperaemia in 23 cases. Limbal follicles were noted in 2 and a moderate ecchymosis in 1 (Fig. 2). The palpebral conjunctiva showed moderate to severe hyperaemia and papillary hypertrophy in 21 cases

Table 1 *Prevalence and severity of symptoms at first visit in 25 cases of herpetic follicular conjunctivitis*

	Severity		
Symptoms	*Mild*	*Moderate*	*Severe*
Swelling of lids	7	5	1
Hyperaemia	11	13	0
Lacrimation	7	9	2
Discharge	15	6	0
Grittiness	11	5	0
Itching	6	2	0
Photophobia	4	2	1
Pain	4	1	0
Blurred vision	6	1	0

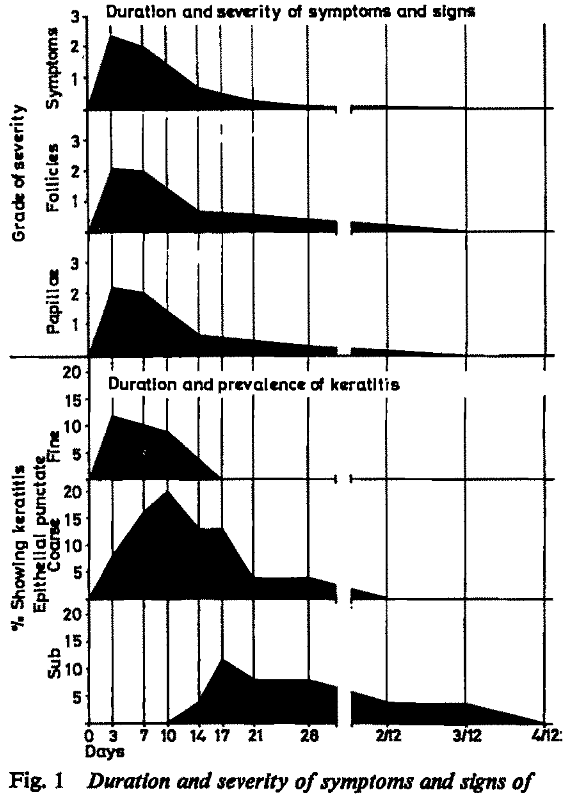

Fig. 1 *Duration and severity of symptoms and signs of disease in 25 cases of acute herpetic follicular conjunctivitis and keratoconjunctivitis*

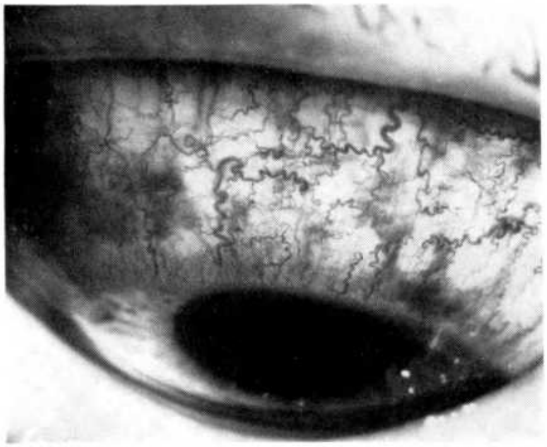

Fig. 2 *Moderate ecchymosis in a case of acute herpetic follicular conjunctivitis*

and moderate to severe follicular reaction in 19 (Table 2). Papillary hypertrophy was most severe in the upper tarsus as well as the lower lid (Figs. 3, 4, 5) and lasted for 2 to 12 weeks (Fig. 1). Follicular reaction was present in all cases. Moderate to severe follicular hypertrophy was present mainly in the lower and upper fornices (Figs. 6, 7, 8). The follicles were small, discrete, and lasted 2 to 8 weeks (Fig. 1).

Nine of the 25 cases developed moderate coarse epithelial punctate keratitis (Jones, 1962). This was generally preceded by fine punctate keratitis (Jones, 1962). In 5 cases mild to moderate subepithelial punctate keratitis (Fig. 9) resembling that of epidemic keratoconjunctivitis (Jones, 1962) developed. The opacities were coarse, fewer than 15 in number, and mainly located in the interpalpebral fissure. The average time from the onset of symptoms to the occurrence of subepithelial lesions was 17 days (Fig. 1). The subepithelial punctate keratitis persisted between 1 and 4 months.

In 2 cases small dendritic ulcers developed on days 4 and 9 respectively. They both responded well to therapy with idoxuridine 0·5% eye ointment. Of the cases with keratitis 2 developed a mild uveitis which responded quickly to therapy with trifluorothymidine 1% eye drops.

PATHOLOGY

In all, 38 conjunctival specimens were collected from 25 patients. In 22 of 25 cases herpes simplex virus was isolated in HEp2 cells.

Of the 24 specimens collected during the first week of infection 21 (88%) were positive for herpes

Table 2 *Prevalence and severity of signs in the palpebral conjunctiva at first visit in 25 cases of acute herpetic follicular conjunctivitis*

	Severity		
Sign	*Mild*	*Moderate*	*Severe*
Hyperaemia	8	13	4
Papillary hypertrophy	4	12	9
Follicular hypertrophy	6	15	4

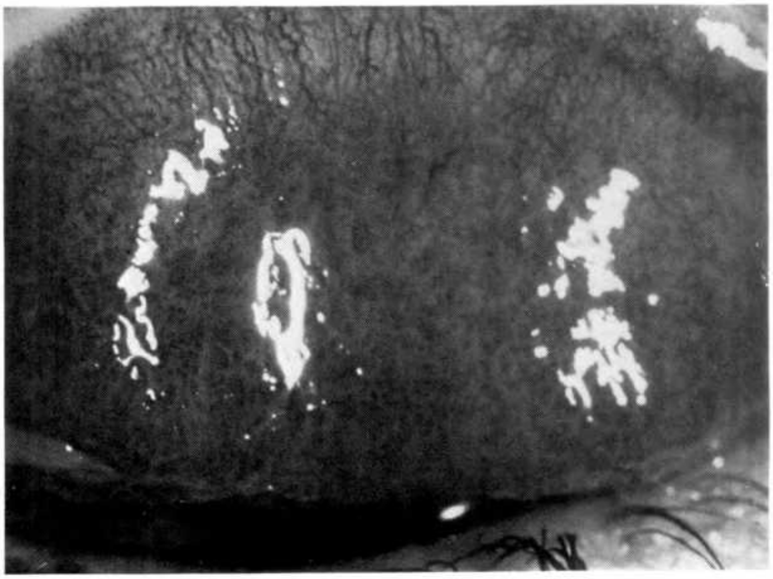

Fig. 3 *Severe papillary reaction in upper tarsal conjunctiva in the first week of acute herpetic follicular conjunctivits*

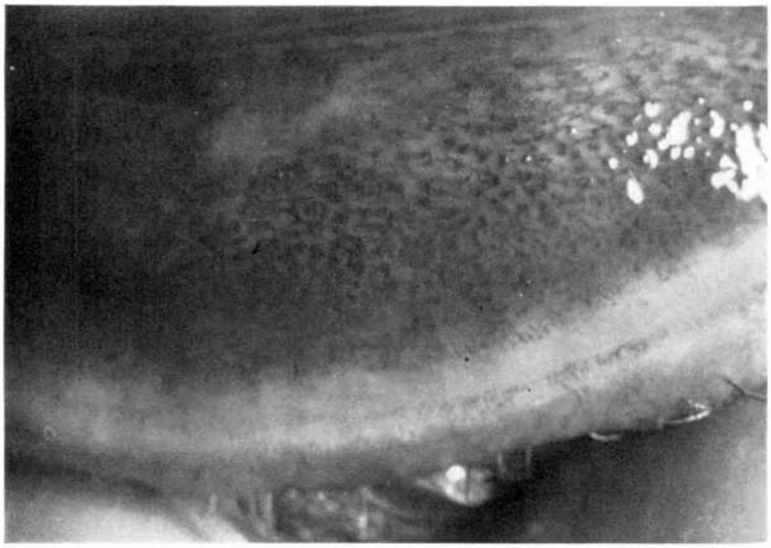

Fig. 4 *Severe papillary reaction in lower lid conjunctiva in the first week of acute herpetic follicular conjunctivitis*

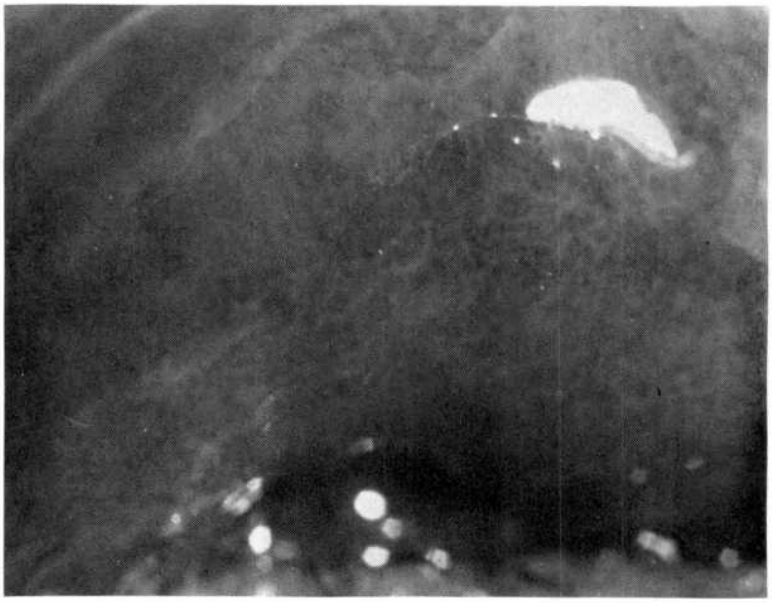

Fig. 5 *Severe papillary reaction in upper fornix conjunctiva in the first week of acute herpetic follicular conjunctivitis*

virus but only 4 out of 10 specimens collected during the second week gave positive results. No virus was isolated after the 11th day of infection. Adenovirus was not isolated from these patients.

Paired or triplicate sera were tested in 14 cases. A 4-fold or greater rise in the level of herpes simplex virus antibody was observed in 4 cases. In 3 of these no herpes virus was isolated. In 1 case in which the conjunctival swab was positive for herpes virus a 4-fold rise in adenovirus antibody titre was obtained.

Conjunctival impressions taken from 7 patients during the course of their disease showed a mixed population of inflammatory cells in which polymorphonuclear cells and monocytes were evenly distributed. No multinucleated epithelial cells were observed in these impressions.

TREATMENT

With a preliminary diagnosis of an adenovirus infection all patients were initially treated with eye drops or eye ointment of chloramphenicol, genta-

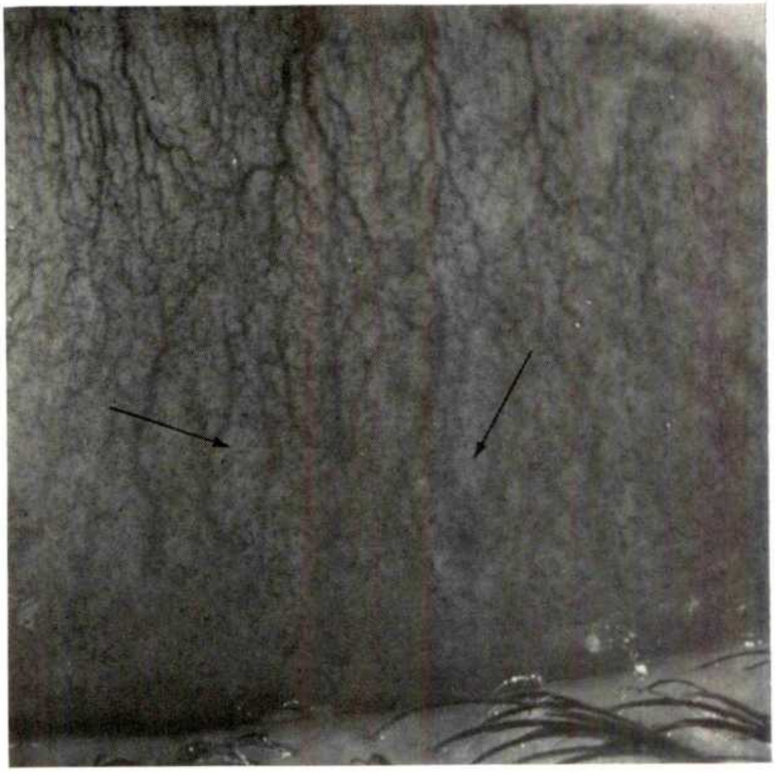

Fig. 6 *Follicular reaction in upper tarsal conjunctiva in the second week of acute herpetic follicular conjunctivitis*

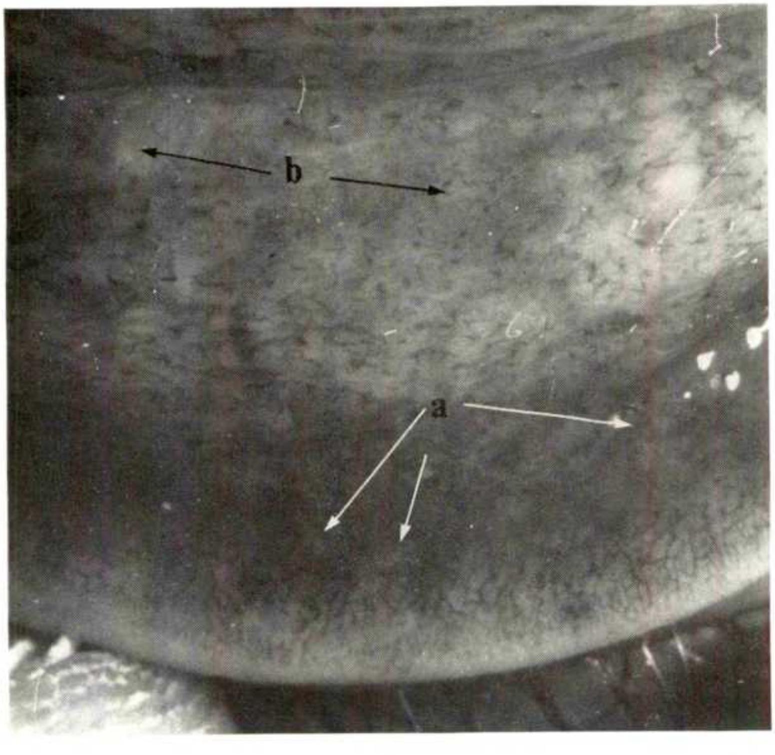

Fig. 7 *Follicular reaction in* (a) *tarsal and* (b) *fornix area of the lower lid conjunctiva in the second week of acute herpetic follicular conjunctivitis*

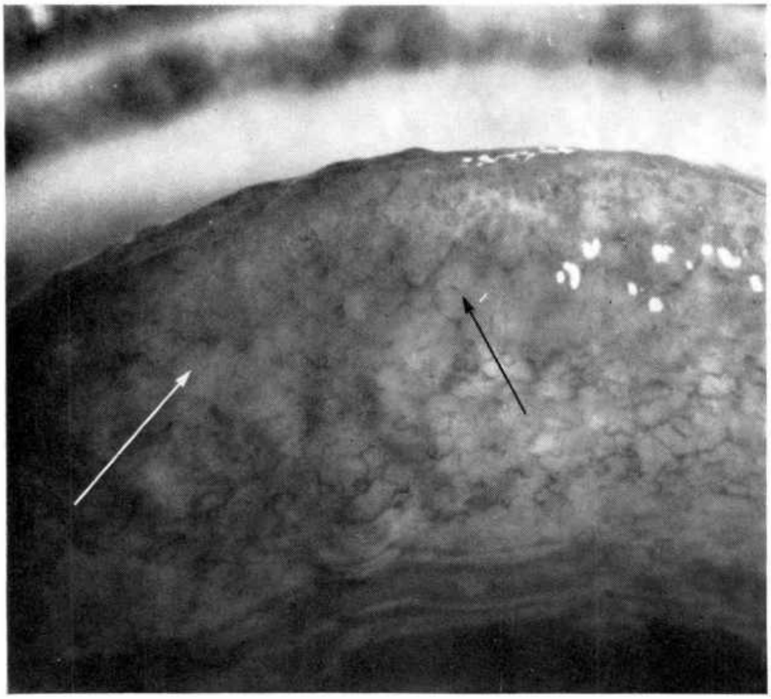

Fig. 8 *Follicular reaction in upper fornix conjunctiva in the second week of acute herpetic follicular conjunctivitis*

micin, or neomycin to prevent bacterial infection. In 12 patients with mild to moderate follicular conjunctivitis treatment with antibiotics was continued. The symptoms and signs in these patients disappeared in 2 to 4 weeks.

In 6 patients who subsequently developed lid lesions or corneal ulcer suggestive of herpetic infection the treatment was changed to idoxuridine eye ointment 5 times daily.

In the other 7 patients with moderate to severe keratoconjunctivitis who had not benefited from the antibiotics the treatment was changed to a 7-day course of trifluorothymidine 1% eye drops (TFT) hourly for the first day, 2-hourly for the second day, and 5 times daily for the next 5 days. In this group the symptoms declined in 2 to 3 days and had completely disappeared in 4 to 5 days. The duration of keratoconjunctivitis in this group was 3 to 4 weeks.

Discussion

Primary herpes simplex ocular infection is a common entity and may constitute one-quarter of all cases of acute follicular conjunctivitis attending ophthalmic outpatient clinics (Jones, 1959) when other causes are not epidemic. The infection occurs predominantly in early life and is generally associated with herpetic lesions on the face, lids, or the cornea.

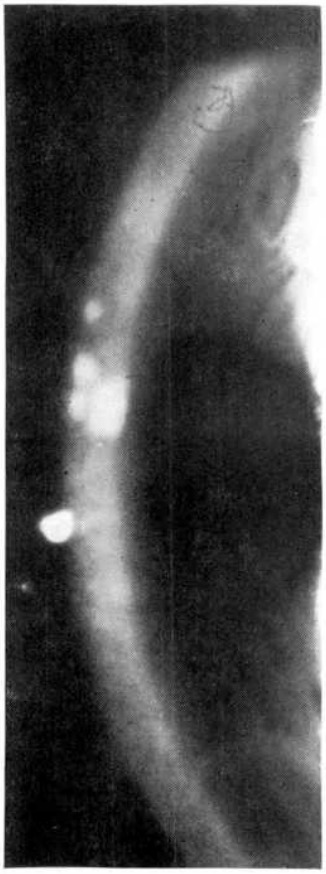

Fig. 9 *Macrophotograph (× 20) of coarse subepithelial punctate corneal opacities in the broad slit-lamp beam*

Herpes simplex virus has occasionally been isolated from cases of acute follicular conjunctivitis with punctate keratitis resembling adenovirus keratoconjunctivitis. Maumenee *et al.* (1945) reported isolation of herpes simplex virus from a patient with bilateral keratoconjunctivitis with no evidence of dendritic ulcers or facial herpetic lesions. Jawetz *et al.* (1955) isolated herpes simplex virus in 2 patients with acute keratoconjunctivitis. Both these patients, however, were also shown to have a rising titre against adenovirus type 8. Jones (1962) found 3 cases of primary herpetic conjunctivitis without lid disease. More recently Knopf and Hierholzer (1975) found evidence of herpes simplex infection in 2 cases which were initially diagnosed as epidemic keratoconjunctivitis. In 1 of these there was serological evidence of concurrent infection with adenovirus type 7.

Concomitant ocular infections with adenovirus and herpes virus may suggest that adenovirus infection may reactivate the latent herpes virus (Nesburn *et al.*, 1967) or chronic infection with low-grade multiplication of herpes virus (Kauffman *et al.*, 1968). However, in the present series of patients the cultural and serological tests for the diagnosis of adenovirus infection were all negative except in 1 patient, indicating that in 24 out of 25 patients the herpes simplex virus was responsible for the ocular disease.

The clinical and epidemiological features of acute herpetic conjunctivitis—moderate to severe papillary and follicular reactions with epithelial and subepithelial punctate keratitis but with little systemic disease—are, in the absence of typical facial and corneal lesions of herpes virus, closely similar to adenovirus infections, including types 8 and 19 keratoconjunctivitis (Jones, 1962; Darougar *et al.*, 1977a). It is therefore important in cases of acute follicular conjunctivitis to consider herpes simplex virus as a possible cause of the disease and to determine the diagnosis with laboratory tests. This is especially important if corticosteroids are at risk of being administered.

In this study HEp2 cells were used for isolation of herpes virus and adenovirus. Studies by McSwiggan *et al.* (1975) have shown that the sensitivity of this cell line is similar to that of HEK cells for the isolation of herpes virus and adenovirus from the eye, though the development of CPE is markedly slower in HEp2 cells. The high isolation rate of 88% obtained in specimens collected during the first week of infection in the present series indicates the importance of early collection of specimens for the diagnosis of ocular herpetic infection.

In contrast to adenovirus, herpes simplex virus is sensitive to various antiviral compounds, including idoxuridine, trifluorothymidine, and adenine arabinoside. It is therefore essential for correct management of this infection to establish an early virological diagnosis to provide a rational approach to therapy.

The authors are indebted to their colleagues at Moorfields Eye Hospital for referring the patients and to the Audio-Visual Department of the Institute of Ophthalmology for help in preparation of photographs.

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References

Darougar, S., Quinlan, M. P., Gibson, J. A., Jones, B. R., and McSwiggan, D. A. (1977a). Epidemic keratoconjunctivitis and chronic papillary conjunctivitis in London due to adenovirus type 19. *British Journal of Ophthalmology*, **61**, 76–85.

Darougar, S., Viswalingam, M., Treharne, J. D., Kinnison, J. R., and Jones, B. R. (1977b). Treatment of TRIC infection of the eye with rifampicin or chloramphenicol. *British Journal of Ophthalmology*, **61**, 255–259.

Gordon, F. B., Harper, I. A., Quan, A. L., Treharne, J. D., Dwyer, R. St. C., and Garland, J. A. (1969). Detection of Chlamydia (Bedsonia) in certain infections in man. I. Laboratory procedures: comparison of yolk-sac and cell culture for detection and isolation. *Journal of Infectious Diseases*, **120**, 451–462.

Jawetz, E., Kimura, S., Hanna, L., Coleman, V. R., Thygeson, P., and Nichols, A. (1955). Studies on the etiology of epidemic keratoconjunctivitis. *American Journal of Ophthalmology*, **40**, 200–211.

Jones, B. R. (1959). The management of ocular herpes. *Transactions of the Ophthalmological Societies of the United Kingdom*, **79**, 425–437.

Jones, B. R. (1962). Adenovirus infections of the eye in London. *Transactions of the Ophthalmological Societies of the United Kingdom*, **82**, 621–644.

Kaufman, H. E., Brown, D. C., and Ellison, E. D. (1968). Herpes virus in the lacrimal gland conjunctiva and cornea of man: a chronic infection. *American Journal of Ophthalmology*, **65**, 32–35.

Knopf, H. L. S., and Hierholzer, J. C. (1975). Immunologic responses in patients with viral keratoconjunctivitis. *American Journal of Ophthalmology*, **80**, 661–671.

Maumenee, A. E., Hayes, G. S., and Hartman, T. L. (1945). Isolation and identification of the causative agent in epidemic keratoconjunctivitis (superficial punctate keratitis) and herpetic keratoconjunctivitis. *American Journal of Ophthalmology*, **28**, 823–839.

McSwiggan, D. A., Darougar, S., Rahman, A. F. M. S., and Gibson, J. A. (1975). Comparison of the sensitivity of human kidney cells, HeLa cells and WI38 cells for the primary isolation of viruses from the eye. *Journal of Clinical Pathology*, **28**, 410–413.

Nesburn, A. B., Elliott, J. H., and Leibowitz, H. M. (1967). Spontaneous reactivation of experimental herpes simplex keratitis in rabbits. *Archives of Ophthalmology*, **78**, 523–529.

Thatcher, R. W., Darougar, S., and Jones, B. R. (1977). Conjunctival impression cytology. *Archives of Ophthalmology*, **95**, 678–681.

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Correspondence

Iritis in Reiter's disease: an example of the Auer principle

TO THE EDITOR, *British Journal of Ophthalmology*

SIR, Auer (1920) noted the effects of local inflammation in serum sickness. Xylol was used to produce local inflammation in the ear of a rabbit with serum sickness, and the animal was then given a repeat injection of serum. The treated ear became inflamed and gangrenous, while the other ear remained unaffected. Similar experiments were carried out in a rabbit's eye (Gamble *et al.*, 1970), where, after an intravenous dose of bovine serum albumin (BSA), 1 eye was given an intravitreous injection of endotoxin. Local inflammation was produced, and when it had resolved a further parenteral injection of BSA produced an acute iritis only in the eye injected with endotoxin. One explanation put forward for these reactions was that under appropriate conditions circulating immune complexes localised into that area associated with inflammation.

Acute iritis is a recognised complication of Reiter's disease, occurring in 8% of patients (Csonka, 1972), but its cause is unknown. We would like to report a case of Reiter's disease whose development of iritis may be an example of Auer's principle.

CASE REPORT

A 44-year-old male, HLA B27 positive, was diagnosed as having Reiter's disease in 1958 when he developed urethritis, conjunctivitis, and arthritis, the latter involving the knees and ankles. He was troubled with recurrent iritis in the right eye in 1958, 1963, and 1967, for which he was treated with a partial iridectomy in 1967. In 1971 he developed low back pain and at that time was noted to have radiological changes of bilateral sacroiliitis and ankylosis of the thoracolumbar spine. In 1972 he developed further arthritis in the knees and ankles, which settled with non-steroidal anti-inflammatory drugs. In May 1977 he receved a blow over the right eye and developed bruising of the eyelids but no obvious local damage to the eye. Five days later he developed an acute iritis, which resolved after 2 weeks' treatment with topical corticosteroids. At that time his peripheral joints were inactive, he had minimal back pain, and his therapy was indomethacin 100 mg a day. Laboratory investigations showed an erythrocyte sedimentation rate (ESR) of 10 mm in 1 hour, C-reactive protein 1·44 mg/100 ml (normal <0·8 mg/100 ml), and circulating immune complexes as detected by the method of Hay *et al.* (1976) were greater than 3 standard deviations above the normal range. Six months later he had only bilateral Achilles tendonitis, and there had been no further attacks of iritis. The ESR was 41 mm in 1 hour, C-reactive protein 3·1 mg/100 ml, and circulating immune complexes remained elevated.

COMMENT

This was the first attack of iritis experienced by this patient in 10 years, so that its occurrence following the blow over the eye is unlikely to be coincidental. Gamble *et al.* (1970) concluded that damage to the uveal vasculature appeared to be necessary to facilitate deposition of circulating immune complexes and the development of iritis. Concussion to the iris, no matter how small, produces vascular changes in the uveal vessels. These consist initially of an ischaemic spasm, followed by a prolonged reactive vasodilatation and hyperaemia of the uveal tract (Duke-Elder, 1972).

Compared with normal controls this patient had elevated levels of circulating immune complexes, as measured by the solid phase C1q radioimmunoassay, before and after his episode of acute iritis. This patient may be an example of the Auer principle, in that vascular changes occurring after the blow to the eye enabled the deposition of circulating immune complexes in the iris, causing acute iritis. The cause of iritis in Reiter's disease is unknown, but his case leads to speculation that it could be secondary to deposition of circulating immune complexes.

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References

Auer, J. (1920). Local autoinoculation of the sensitized organism with foreign protein as a cause of abnormal reactions. *Journal of Experimental Medicine*, 32, 427–446.

Gamble, C. N., Aronson, S. B., and Brescia, F. S. (1970). Experimental Uveitis. I. The production of recurrent immunological (Auer) uveitis and its relationship to increased uveal vascular permeability. *Archives of Ophthalmology*, 84, 321–330.

Csonka, G. W. (1972). Reiter's disease. *British Journal of Hospital Medicine*, 7, 8–12.

Hay, F. C., Nineham, Lynn, J., and Roitt, I. M. (1976). Routine assay for the detection of immune complexes of known immunoglobulin class using solid phase C1q. *Clinical and Experimental Immunology*, 24, 396–400.

Duke-Elder, S. (1972). *System of Ophthalmology*, 1st edn. Vol. 14, p. 89. Henry Kimpton: London.

Notes

Search

The Applied Vision Association and the Ergonomics Society will hold a symposium on 'Search and the human observer' at Loughborough University of Technology on 3–5 January. Further details from Murray Sinclair, University of Technology, Loughborough, Leics LE11 3TU (Tel. Loughborough (0509) 63171, ext. 392).

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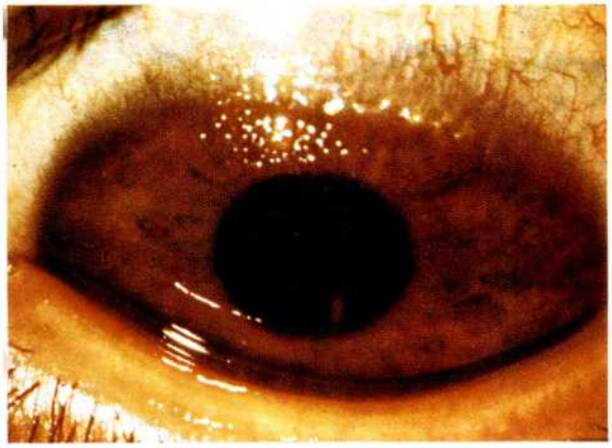
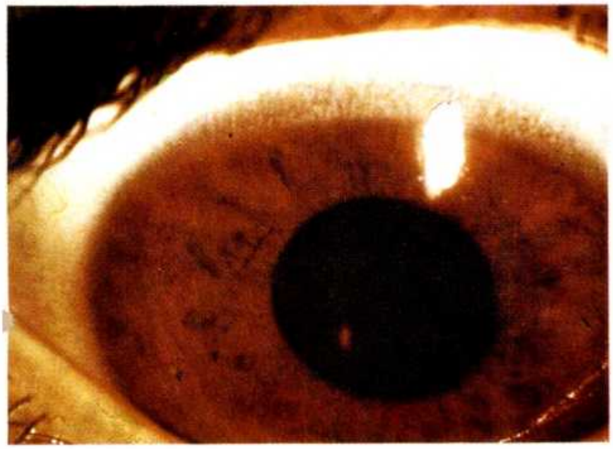
In his eyes, allergy is much more than a minor irritation.



a. The superior limbus in a placebo treated eye of a patient suffering from vernal kerato-conjunctivitis, stained with fluorescein. Note the limbal hyperaemia and swelling and the irregularity of the corneal surface.



b. The opposite eye of the same patient treated with sodium cromoglycate eye drops. Before treatment, both eyes appeared similar.

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